Archives of Dermatology and Syphilology

VOLUME 5 JANUARY, 1922 NUMBER 1

THE TREATMENT OF ANTENATAL AND CONGENITAL SYPHILIS *

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The problem of antenatal and postnatal syphilis is one of the largest in the entire field of medicine, not only because it concerns nearly every specialty, but also because of its wide social and economic importance. As is well-known, syphilis is the most frequent cause of abortions and stillbirths, statistics ranging from 20 to 50 per cent. Williams, in his series of 10,000 pregnancies, holds the disease responsible for 26 per cent. of the fetal deaths between the end of the seventh month of gestation and the two weeks prior to delivery. Routh arrived at about the same figures in his computations, stating that, in urban populations, 25 per cent. of the miscarriages and stillbirths are due to this infection. When the fetus survives and is brought into the world, suffering from latent or active syphilis, its personal handicaps, as well as its being a burden to the family and, only too often, to the community, have to be reckoned with.

We are, however, more optimistic for the future because our more efficient methods of treatment and investigation are reducing not only fetal mortality but also the number of cases of active congenital syphilis. We have cooperated for some time with a number of maternity institutions, and the infrequency of actively syphilitic infants has been a matter of surprise to us. The explanation, of course, is simple. Practically all maternity hospitals today are thoroughly investigating their prospective patients to determine the presence of a syphilitic infection. A careful history is taken as to the outcome of previous pregnancies and a blood examination is made in all cases. Even where the serologic findings are negative, if there is any suspicion of the disease, syphilitic treatment is given, it being believed better to err on the side of safety. At the Vanderbilt clinic, we have had a great many women referred to us with positive blood reactions. Some give a history of infection dating from the time of their marital ties, but by

* Read at the Forty-fourth Annual Session of the American Dermatological Association, at Swampscott, Mass., June 2-4, 1921.

far the larger number can supply no such data. In these, the most frequent story is one of repeated abortions or miscarriages, followed later by a stillborn child or the birth of a premature infant which died shortly after from malnutrition and feeble development. We make it a rule in cases in which the only symptom is a positive serum reaction to have the test corroborated in different laboratories, as we are fully aware of the danger of relying on one laboratory examination and of the fact that a normal pregnant woman's blood may give a strongly positive reaction with the cholesterinized antigen.

We have found that from 25 to 35 per cent. of the patients referred to us by maternity hospitals, because of a strongly positive reaction with cholesterinized antigen alone give a negative Wassermann reaction with all methods when they report several weeks after delivery and remain negative on repeated examination.

THE IMPORTANCE OF EARLY TREATMENT

Does treatment early in pregnancy prevent abortions or miscarriages and insure the birth of a healthy nonsyphilitic infant? We can answer this question in the affirmative. It is important, however, to begin treatment early. Little can be expected if we delay until the last weeks of gestation, as illustrated by the subjoined case:

CASE 1.—*History.*—R. E., colored, aged 19, pregnant seven months, was referred to the clinic Feb. 2, 1921, for treatment. She gave no history of infection, had had no abortions and presented only a ++++ Wassermann reaction. She received four injections of arsphenamin, 0.3 gm. at weekly intervals, and mixed treatment. February 21, she gave birth to a girl weighing 4 pounds and 2 ounces (1870 gm.). The blood from the cord gave a ++++ reaction; and ten days later, from the heel, a ++++ reaction. The physician in charge reported that at birth the liver and spleen were not palpable.

The infant did not gain in weight. When the infant was 42 days old, a small ulceration appeared on the labium majus and oozing of blood was observed from the small stab in the left heel, which had never closed. The child now became distinctly jaundiced, vomited, and had gray, chalky stools; the spleen was enlarged, and the liver slightly enlarged; the heart and lungs were negative. On the forty-fourth day, whole blood was injected subcutaneously, but the bleeding continued from the heel and labium and two hematomas appeared above the knees. Blood examination revealed: hemoglobin, 65 per cent.; red blood cells, 3,650,000; white blood cells, 12,200; polymorphonuclears, 52 per cent. On the forty-sixth day, the infant died.

Necropsy Findings.—We are indebted to Dr. W. C. Johnson, pathologist to the Sloane Hospital, for the necropsy report. Baby E., girl, aged 46 days; weight 1,950 gm.; length 46 cm. Anatomic Diagnosis: (1) congenital syphilis, (2) syphilitic hepatitis, (3) syphilitic splenitis, (4) anemia, (5) jaundice, (6) melena, (7) injected blood (therapeutic), (8) ulcer of labium, (9) involution of thymus, (10) hemorrhage in parathyroids, and (11) fractures of ribs (6, 7, 10, right side).

The body was that of a poorly nourished, apparently full-term infant. Rigor and lividity were present. The skin was pale and markedly jaundiced. The scalp, eyes and ears appeared normal. There was no discharge from the nose, and no fissures around the mouth. The anus was normal. There was a small yellow patch with a blackish crust on the left labium majus. The navel appeared completely healed and normal.

There was no fluid or exudate in the peritoneal cavity. The umbilical vein was still open. The mesenteric lymphnodes were enlarged.

The pleural cavities were normal. There was a large collection of clotted blood in the left pectoralis major. The muscles were pale. The pericardial cavity contained a normal amount of clear, bile tinged fluid.

The thymus weighed 1½ gm., was very soft and had much loose tissue around it.

The heart was normal in size, and there were no epicardial hemorrhages. The muscle was pale. The foramen ovale still showed a small opening and the ductus arteriosus was not fully closed. There were no valvular lesions.

The lungs weighed 40 gm. They appeared well aerated. There were no pleural hemorrhages. Both lungs felt soft, crepitated slightly, and were pale white except for small, reddish patches along the posterior part of the lower lobes. There was slight emphysema along the anterior margins. The trachea and bronchi contained reddish brown, slimy material.

The thyroid was pale and rather small.

The parathyroids were all enlarged and dark red, possibly hemorrhagic.

The tongue appeared normal.

The esophagus contained reddish brown material resembling partly digested blood. This appears to be the same material as that in the trachea.

The stomach contained bloody material.

In the small intestines, there was blood stained mucous throughout the lower 68 cm.

The pancreas was not enlarged.

The spleen was markedly enlarged, weighing 42 gm. The capsule was smooth and tense. The cut surface was rather firm and dark red.

The liver was slightly enlarged, weighing 129 gm. The capsule revealed a few patches of thickening. The cut surface was greenish brown, fairly uniform in appearance. The gallbladder and ducts appeared normal.

The suprarenals together weighed 3 gm., and showed no hemorrhages.

The kidneys together weighed 21 gm. The surfaces were pale. The cut surfaces showed a slightly thickened cortex, but were otherwise normal.

The ureters were slightly dilated at their upper parts. The bladder, uterus and adnexa were normal.

The epiphyseal lines at the knee joint were slightly thickened and bile-stained.

The spinal cord appeared normal.

The brain was pale but otherwise normal.

The sixth, seventh and tenth ribs on the right side were fractured and showed some callus formation.

The middle ears, sutures and fontanelles were normal.

Microscopic Examination.—The heart was normal.

Some lobules of the lungs were emphysematous and others atelectatic. In the latter areas, the alveoli contained mononuclear cells and erythrocytes. The alveolar walls generally appeared more cellular and less vascular than normal. There was no definite fibrosis.

The liver cords, which were rather large, were separated by a moderate amount of diffuse cellular fibrous tissue. Some of the liver cords were necrotic and were invaded by polymorphonuclear leukocytes. Many of the hepatic cells contained numerous coarse granules or masses of brown pigment. Some of the hepatic cords had numerous nuclei arranged near their centers, giving them the appearance of giant cells. New blood formation was not increased. The portal canals and their contents revealed nothing significant. The capsule was normal. The capsule of the spleen was slightly thickened. The malpighian bodies were small and indistinct. The pulp presented a very confused picture. The pulp cords were thickened and contained numerous mononuclear cells as well as red cells.

The kidneys were practically normal.

Examination of the suprarenals revealed congestion of the inner part of the cortex and medulla. The cells of the inner part of the cortex were separated from each other.

The pancreas was practically normal. In some places, there was a small amount of interstitial fibrosis.

Examination of the thymus revealed that the lymphoid tissue was considerably diminished and the reticulum was more prominent than normal.

Examination of the thyroid revealed that the acini were well developed and many contained colloid.

There were no changes of any significance in the stomach and intestines.

The uterus was normal.

In the ovaries, there were several rather large, and one cystic follicle.

The fallopian tubes were normal.

In the mesenteric lymphnode, the lymphoid tissue was greatly decreased. The lymph sinuses were packed with large phagocytes, many of which contained lymphocytes.

There was no evidence of inflammation in the navel.

The lesion on the labium was a superficial ulcer with necrosis and slight leukocytic infiltration.

Levaditi Sections: There were no organisms in the kidneys.

Examination of the suprarenals revealed numerous spirochetes in and around the medulla.

No organisms were found in the spleen except a few around one of the larger blood vessels.

A few spirochetes were found in the lungs.

No spirochetes were found in the pancreas.

A few were present in the lymphnodes.

There were very few organisms in the thymus.

In the liver, spirochetes were present in enormous numbers.

The ovary was negative.

In the heart, there were a moderate number of the organisms.

COMMENT

Had this mother been seen during the early period of her gestation and treated systematically, we feel confident that she would have been delivered of a full-term, healthy baby. In the treatment of these patients we follow a regular plan of giving from six to eight injections of arsphenamin or neo-arsphenamin, the former in doses of from 0.3 to 0.4

gm., the latter in doses of from 0.45 to 0.6 gm., at weekly intervals, together with mercuric salicylate or mercuric chlorid, 1 grain, once a week for from twelve to fifteen injections. As a rule, pregnant women tolerate the treatment well and without bi-effects. When the mercurial injections are especially painful or give rise to abdominal cramps, we discontinue them and administer mercury or mixed treatment by mouth. If the remedies are well tolerated, treatment is continued interruptedly during the entire period of pregnancy. Of course, the kidneys and other organs are carefully watched for the development of toxic symptoms. While many of the infants from such mothers are without clinical or serologic evidence of the infection, we have not been able to reduce the positive findings in many of the mothers to negative. The reason for this is that many of them have had their infection a number of years and the usual difficulty to reverse the blood reaction applies here. Infants born of treated mothers have been carefully examined for cutaneous or visceral syphilitic manifestations and have now been followed serologically for years with negative results. Whether they will develop active signs of the disease in later life is a question that time only can decide.

A PROBLEM IN IMMUNOLOGY

How is it possible for a mother with a positive Wassermann reaction to give birth to a baby with a negative reaction? Do our immunologic theories offer an explanation, or does the anatomic barrier interposed by the placenta play the chief rôle? We believe the former offer a more satisfactory solution, and we are not inclined to regard as significant the view that the placenta acts as a filter, because of the contradictory findings presented. To account for a healthy infant which began its development with the strongly positive blood of its mother and continued to be nourished with it during its entire existence in utero, Routh's theory of the action of chorionic ferments might also apply.

According to Williams, a positive maternal blood does not necessarily imply the existence of fetal syphilis, nor do the findings in the fetal blood at birth necessarily give positive information. This, also, has been our experience, for we have seen well-developed infants at birth give a $++++$ reaction with blood from the cord, but ten days later give a negative one, which subsequently remained persistently negative both serologically and clinically. We, therefore, do not believe that we can attach much significance to the reaction at birth in the absence of other data. Williams has also found infants, with a negative Wassermann reaction at birth and a syphilitic placenta, develop a positive reaction later, with clinical manifestations. These

fluctuations in the sero-reaction of early congenital syphilis, therefore, demand a frequent repetition of the test. Occasionally, we see syphilitic babies, with a ++++ Wassermann reaction at birth which becomes negative ten days later and then positive after a week or two, as in the following case:

CASE 2.—*History.*—Baby F. was born in one of the maternity hospitals, of a mother who had a strongly positive Wassermann reaction. At delivery, a specimen of blood was taken from the umbilical cord and sent for serologic examination. This was reported ++++. The infant was a full-term baby but weighed less than 4 pounds (1,800 gm.), and was immediately placed in an incubator. Examination at birth and daily thereafter for a week failed to reveal any lesions of a syphilitic nature. The blood taken from the longitudinal sinus ten days after birth was reported negative. At this time a lesion appeared about the anus and distinct snuffles developed.

There was difficulty in feeding the infant, and its weight had increased slightly. Local rubbings of mercurial ointment were ordered and kept up daily. We saw the child for the first time on the thirty-first day after birth. It weighed then 4 pounds and 2 ounces (1,870 gm.), was feeble and shriveled looking, and had a marked coryza. The skin of the body presented no lesions except around the anus, where an infiltrated annular patch, of dusky red hue, was present. A Wassermann test on that day from the longitudinal sinus was reported ++++ by two different laboratories. On the fifty-seventh day, the infant died.

Necropsy Findings (Report by Dr. Johnson).—Baby F., a boy, aged 57 days, weight 2,000 gm., length 49 cm. Anatomic Diagnosis: (1) acute peritonitis, with inflammation of tunicae vaginales; (2) congenital syphilis (lesions in liver, spleen and pancreas); (3) jaundice, and (4) malnutrition.

The body was that of a poorly nourished colored infant. Rigor mortis was absent. There was slight jaundice. The eyes and ears appeared normal. A whitish material came from the nose. There were no fissures around the nose or mouth. The fontanelles were wide open and the sutures were not closed. The abdomen was distended. The navel appeared normal. The scrotum was large and edematous; the skin over it was slightly reddened. Around the anus were several small, nearly healed fissures. The palms and soles appeared normal. There was some peeling of the epidermis around the wrists, ankles and knees. There were no hemorrhages or eruptions on the skin.

The peritoneal cavity contained a small amount of turbid yellowish fluid in which were lumps and flocculi of whitish material resembling fibrinopurulent exudate. Some of these flocculi were scattered over the coils of the intestine and also on the capsules of the liver and spleen. The serous surfaces were rather dull and pale. There was no localization of the peritonitis, no adhesions, and no local indications of its origin.

The pleural cavities contained no fluid, exudate or hemorrhage.

The pericardial cavity contained a normal amount of fluid showing bile coloration.

The heart was normal in size. The foramen ovale and ductus arteriosus were closed. There were no hemorrhages or valvular lesions.

The lungs were pale pinkish, were well expanded and showed no definite lesions.

The larynx, trachea and bronchi were normal.

The thymus weighed 2.5 gm., was very small but of good consistency

The liver weighed 110 gm., was pale and somewhat jaundiced; otherwise it showed no definite lesions.

The spleen weighed 10 gm. No abnormality was noted.

There were no lesions noted in the gastro-intestinal tract and pancreas.

The kidneys together weighed 29.5 gm. They were pale but showed no other changes.

The suprarenals together weighed 3.5 gm. They appeared very small and showed no lipoid material.

Examination of the genitals revealed that the processus vaginalis still communicated with the peritoneal cavity through a small opening on each side. The cavities were rather large and contained fibrinopurulent material. The tunica vaginalis was thickened. The testes appear slightly swollen and reddened.

The epiphyseal lines at the knee appeared practically normal. In the upper end of the shaft of the tibia on both sides, adjacent to the epiphyseal lines, a small part of the cortex and medulla were replaced by a homogeneous whitish material, softer than the cartilage of the epiphyses. The symmetry of these lesions and the absence of any inflammatory reaction made them appear to be congenital anomalies or defects of development.

There were no gross lesions in the brain. The head was 30.7 cm. in circumference.

Microscopic Examination.—The heart was normal.

In the lungs some lobules were emphysematous; others contained a moderate amount of albuminous precipitate and a few large and small mononuclear cells. There was no fibrosis.

Examination of the liver revealed that the capsule was normal. The portal canals showed an increase of fibrous tissue and slight cellular infiltration. Scattered through the lobules were several small patches of fibrosis. There was no necrosis. There was a considerable amount of blood cell formation.

The kidneys were practically normal.

Examination of the spleen revealed that there was an exudate on the capsule, consisting of fibrin with mononuclear cells and leukocytes. The capsule itself showed a slight leukocytic infiltration. The malpighian bodies were distinct and of moderate size. The venous sinuses were distinct and only partly filled with blood. Many large mononuclear cells containing brown pigment were present. The pulp cords were wide and were packed with red cells. Throughout the pulp there was a definite increase of connective tissue in the form of small strands.

In the suprarenal, the cells in the inner part of the cortex were small and separated. Many were necrotic or autolyzed.

In the pancreas there was a moderate interstitial fibrosis with loose cellular connective tissue. Otherwise the gland appeared practically normal.

In the thymus, the lymphoid cells in the cortex were considerably diminished in number. Large mononuclear cells were relatively abundant.

Examination of the testicles revealed that the serous cells of the tunica vaginalis had disappeared and the surface was covered with a thick layer of fibrin, beneath which the connective tissue was infiltrated with leukocytes and mononuclear cells. The subcutaneous tissue of the scrotum showed edema and the exudate of the fibrin.

Sections of lesions of the anus showed practically nothing but crusts on the surface, beneath which the epithelium had healed.

Levaditi sections of all organs, including the brain and spinal cord, were negative for spirochetes.

COMMENT

This case is interesting because the child had a ++++ Wassermann reaction and syphilitic lesions in the viscera, and yet the examination was negative for spirochetes after a careful search.

It is a common clinical fact that the tendency to transmit the disease lessens with the age of the infection. We frequently see women with strongly positive reactions, who have had no treatment whatever, give birth to healthy offspring with a negative blood reaction or to infants with alternating positive and negative reactions.

STATISTICS IN ONE HUNDRED AND FORTY CASES

We have had under observation, during the last year and a half, 140 children who were born of mothers with a strongly positive Wassermann reaction, but whose own reactions are negative clinically and serologically, the latter on repeated testing.

There were twenty-seven female white children, forty-one female black children, thirty-six male white children, and thirty-six male black children.

The age on admission in eighty-seven children ranged from 3 weeks to 6 months; in the rest from 6 months to 9 years.

The Wassermann reaction of blood from the umbilical cord of twenty-two of the younger infants gave a positive test in nineteen. The Wassermann reaction on admission to the clinic and repeated several times thereafter was negative in all of the 140 children.

Syphilis was admitted by nineteen fathers; it was denied by one or both parents in 121 cases; of these, twelve fathers admitted gonorrhea. The age of the infection when admitted by the father ranged from three to sixteen years. The number of years the parents had been married ranged from less than one year to eighteen years; five of the children were illegitimate.

The Wassermann reaction was obtained in sixty-six of the fathers; in thirty-six it was positive; in thirty negative; of the latter, five had had treatment for syphilis. Seventy-four fathers refused or were unable to come for a test. The Wassermann reaction was positive in all of the mothers; 133 had a ++++ reaction; three had a +++ and four a ++ reaction.

Forty-three mothers gave a history of abortions or stillbirths; ninety-seven gave no history. Sixty mothers had had no other children; sixty-four had other children whose reactions were negative; five had other children who were syphilitic, and eleven had both healthy and

syphilitic children. Forty-eight of these women had had no antenatal treatment; twenty-five had had internal treatment only; sixty-one had had partial treatment with arsphenamin and mercury, and six only had had prolonged treatment with these drugs.

NONSYPHILITIC CHILDREN OF SYPHILITIC PARENTS

The question frequently arises as to what should be done with infants with a negative Wassermann reaction born of parents with a positive Wassermann reaction, and it is difficult at times to render a decision. One often sees the statement that the children of syphilitic parents should be treated whether symptoms are present or not and regardless of a negative Wassermann reaction. This, in our opinion, is an unnecessary hardship, and we favor instead keeping them under surveillance for several years after we have satisfied ourselves, in the absence of clinical manifestations, that the blood and spinal fluid are negative.

Can a patient with a negative Wassermann blood reaction and a positive spinal fluid reaction transmit the disease? In answer we quote the subjoined case.

CASE 3.—Mrs. G. H., white, aged 25, whose previous history was indefinite was delivered at the Sloane Maternity Hospital of a baby weighing 4 pounds and 13 ounces (2,180 gm.). The Wassermann reaction of the blood from the umbilical cord was + + + +. Examination by the resident physician at birth revealed no evidence of syphilis. The blood from the longitudinal sinus ten days later was strongly positive. The baby had now developed distinct snuffles and an eruption on the buttocks consisting of lesions of various types, impetiginous, bullous and infiltrated papules. There were no anal or mouth lesions. The clinical diagnosis was in favor of syphilis. Another specimen of blood was sent to two different laboratories and again reported strongly positive. The mother's blood before delivery and after the birth of the child was negative; twenty days later, examined in two different laboratories, it was again reported negative. Clinical investigation failed to disclose any signs of syphilis. She was then given a provocative injection of arsphenamin, but the blood remained negative. A spinal puncture was now made and the fluid found positive in all phases.

As she had been deserted by her husband some time before entering the hospital, we were unable to extend our investigations to him. In this instance, of course, we cannot exclude paternal syphilis. Again, it is possible that the mother was suffering from an old neurosyphilis, the infection dating prior to her marriage, although she disclaimed any knowledge of it.

QUESTION OF LIKELIHOOD OF TRANSMISSION IN NEUROSYPHILIS

Are patients with neurosyphilis more likely to transmit the disease to their offspring than those in whom the nervous system is spared? We think not. This we judge from the large number of cases we have observed in which both wife and children had escaped infection. Most of these patients, however, had not married until quite an

interval had elapsed since their infection, namely, from ten to fifteen years. On the other hand, a case such as the one presented herewith is not unusual:

CASE 4.—Mr. J. W., white, aged 35, acquired syphilis at the age of 18, for which inunction treatment was carried out in a systematic fashion for two years. He married at the age of 22, his wife giving birth two years later to a healthy child. He is at present under treatment for an advanced tabetic condition, with all the signs of degenerative changes in the posterior columns of the cord. His blood Wassermann reaction is strongly positive and the spinal fluid is also strongly positive in all phases. He has four children, 11, 8, 5 and 3 years of age. The youngest was born after the patient had complained of neurologic symptoms. They are all negative clinically and serologically. The wife also had a negative Wassermann reaction both in the blood and the spinal fluid.

QUESTION OF MARRIAGE

When is it safe for a patient who has had a syphilitic infection to marry? From our experience in the past, we believe a person who has had active syphilitic treatment, is free from all clinical evidence, has a negative spinal fluid and whose blood has been negative for two years may be permitted to marry. Recently, we were called on for an opinion in the subjoined case:

CASE 5.—P. Y. was under our care for an extragenital infection acquired about six years previously. The chancre was not recognized, and he was treated surgically until secondary manifestations made their appearance, at which time we first saw him. He received arsphenamin and mercuric salicylate, in all twenty intravenous injections and thirty intramuscular injections in two courses. The Wassermann reaction had been negative for more than five years, tests having been taken at six-month intervals after the second year. He was instructed to have a lumbar puncture, but for business and family reasons he was unable to have this done. He then married, and his wife recently gave birth to a premature baby, weighing about 5 pounds (2,260 gm.). The skin, mucous membranes and viscera were carefully examined for clinical evidence of syphilis, but none was found. A specimen of blood was not taken by the attending physician for fear of arousing the mother's suspicions. However, the placenta was sent to a private laboratory for microscopic examination and the pathologist reported that he found spirochetes in the tissue.

COMMENT

With all the negative data we have in the father's case, we are inclined to doubt the accuracy of the report. We are told by pathologists with experience in placental tissue work that it is an exceedingly difficult task to find spirochetes and that often one is not rewarded until hundreds of sections have been studied, even when active manifestations of the disease are present in the child. There, of course, remains the possibility that the mother was syphilitic. This was ruled out only clinically, but in the case of the child there was likewise no

clinical evidence of the disease, other causes besides syphilis being responsible for prematurity. Would it be possible for a husband whose Wassermann reaction has been repeatedly negative for five years to infect his wife? We do not deny that a patient may harbor spirochetes in the testicles and have a negative blood reaction, but we are not inclined to believe that one who has been treated thoroughly and whose blood has been continuously negative for five years is likely to transmit the disease.

DEMONSTRATION OF SPIROCHETES IN PLACENTA

To illustrate how difficult it is to demonstrate spirochetes in the placenta even when they are abundant in the viscera, Dr. Johnson's report on Baby A. is appended.

CASE 6.—*History.*—The child, a boy, was born at the eighth month of gestation of a mother and father having strongly positive Wassermann reactions, and lived only four days. It weighed 1,700 gm. The anatomic diagnosis was: (1) congenital syphilis; (2) maceration, and (3) prematurity.

Necropsy Findings.—The body was well developed and showed no external abnormalities except softening of the head, and peeling of the epidermis in places over the trunk and extremities. Rigor mortis was absent.

The peritoneal cavity contained some reddish brown fluid.

The pleural cavities were normal.

The pericardial cavity contained a normal amount of fluid, which was rather turbid.

The thymus was small and soft.

The heart was normal in size and showed no lesions except that the myocardium was pale and soft.

The lungs were normal in size, pale, soft and not aerated.

The thyroid gland was normal.

The gastro-intestinal tract showed no gross lesions.

The pancreas showed no gross lesions.

The spleen was much enlarged, pale, brownish-red in color. On the capsule there was a slightly whitish coating, apparently fibrin. The cut surface was brownish red and rather soft.

The liver was slightly enlarged and quite soft. On section, the cut surface had a uniform pale brownish-red color.

The gallbladder and ducts were normal.

The suprarenals showed no gross lesions.

The kidneys were pale, but otherwise normal.

The ureters and bladder were normal.

The testicles were in the scrotum and appeared grossly normal.

The epiphyseal lines at the lower end of the femur and the upper end of the tibia did not appear widened or irregular, but there was a yellowish discoloration extending for some distance into the marrow of the shaft.

The brain was very much softened and no gross lesions could be found.

Microscopic Examination.—The organs for the most part manifested advanced decomposition and could hardly be recognized histologically. The lung showed

slight thickening of the interalveolar septums, which appeared edematous rather than fibrous. The alveolar epithelium was not recognizable. Many alveoli contained a network of fibrin threads.

Levaditi Sections: Spirochetes were present in large numbers in the lung, liver, spleen and suprarenal. The pancreas showed a moderate number.

On cross examination the placenta, which weighed 400 gm. (nearly one-fourth of the weight of the fetus), appeared pale and was thicker than normal in proportion to its size. No macroscopic infarcts or calcified areas were noted. The umbilical cord was thick and appeared edematous.

Microscopic examination of the placenta revealed that the chorionic villi, teased out in salt solution, appeared thicker and less vascular than normal. Stained sections showed the villi enlarged, with greatly diminished vascularity and an infiltration of the stroma with a moderate number of mononuclear cells. Levaditi sections which were stained along with the fetal organs showed no spirochetes in the placenta, umbilical cord or fetal membranes.

Diagnosis.—Syphilis of the placenta was diagnosed.

METHOD OF TREATMENT

Since our preliminary report in November, 1920, on the treatment of congenital syphilis with intramuscular injections of neo-arsphenamin and mercuric chlorid, our confidence in the method has grown, and we are decidedly encouraged as to the ultimate outcome in these small patients. Our work has been greatly hampered because of the enormous difficulties encountered in obtaining the cooperation of mothers as to reporting weekly. After active lesions have disappeared and the child looks healthy and gains in weight, indifference sets in or the address is changed to another quarter of the city, and the visits are discontinued. In spite of efficient social service and follow-up work, treatment has been interrupted in a number of cases, or we have failed to induce the mothers of new patients to begin treatment. If we had had hospital facilities we feel that more might have been accomplished, and our natural timidity in increasing the dosage might have been overcome sooner.

From the results obtained, however, we believe that it is the method of choice. We are led to this belief by the rapid disappearance of all clinical signs, the improvement in the nutrition of the child, its steady gain in weight and the reversal of a positive Wassermann reaction to negative. In the literature one frequently sees the claim that a positive Wassermann reaction in congenital syphilis cannot be changed. Of forty-seven children with positive reactions who have received one course or more of treatment, fourteen gave negative reactions on repeated examination. Among those who still gave a ++++ reaction, we have several in whom the blood became negative after one course of treatment and then positive again after the period of rest. In the case of the older children, the reaction is not so easy to influence. The same problems, therefore, present themselves as in the adult with

acquired syphilis. The infection must be attacked early and treatment must be prolonged to bring about a continuously negative Wassermann reaction.

Originally we gave 0.075 gm. of neo-arsphenamin to infants from 3 to 8 weeks old, at weekly intervals; 0.1 gm. from 2 to 6 months; 0.15 gm. from 6 months to a year, and from 0.15 to 0.2 gm. from 1 to 2 years, in a course of six injections, followed by a rest period of from four to six weeks. We are now giving from six to eight injections to the course and make the initial dose 0.1 gm. for infants from 2 to 12 weeks old; 0.15 gm. from 3 months to 9 months; 0.2 gm. from 1 to 2 years, and 0.25 to 0.3 gm. for children 3 years old. The mercuric chlorid, too, we have increased to from ten to twelve injections to the course, at intervals of a week, and the dosage as follows: 1/10 grain for children from 2 weeks to 6 months old; 1/8 grain from 6 months to 1 year; 1/7 grain from 1 to 2 years; 1/5 grain from 2 to 3 years, and 1/4 grain for those more than 3 years old.

Just as in acquired syphilis, the treatment must be individualized and the intervals lengthened or the dosage changed if indications arise. The urine should be examined at frequent intervals, as occasionally a trace of albumin is found, but this quickly subsides when the drug is discontinued. We believe two full courses each, with proper intervals, should be given, regardless of a negative reaction, and possibly a third course of mercury. In very feeble infants, it is better to initiate the treatment with mercury, giving about eight injections before the administration of neo-arsphenamin.[1] To date, we have had no abscesses even in undernourished infants with a poorly developed musculature. No reactions from the drugs have been noted in the dosage given, except an occasional trace of albumin after the mercury.

The eye, neurologic and spinal fluid examinations should be carried out as in the case of adults.

SUMMARY OF EIGHTY-EIGHT CASES

We summarize herewith the data on the cases of eighty-eight children who have come to us within the last fifteen months with evidence of syphilis.

There were eighty-eight children with clinical or serologic evidence of syphilis: thirty-four female, white; eighteen, female, black; twenty-six male, white, and ten male, black.

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1. It is important to use neo-arsphenamin which is especially prepared for intramuscular injection and is neutral in reaction. That put up for intravenous use is slightly alkaline and when injected into gluteal muscles is apt to be followed by tissue necrosis or abscess formation.

We would also like to emphasize the necessity of using only sharp needles for these treatments. As a rule, they are not sharp enough when delivered by the manufacturers and should be sharpened on a fine oil stone by the operator.

The age, on admission, in twenty-three ranged from 3 weeks to 6 months; in eight from 6 to 12 months; in fourteen from 1 to 2 years; in forty-three from 2 to 12 years. The Wassermann reaction obtained from the blood of the cord in nine of the infants was + + + +.

The Wassermann reaction on admission to the clinic was positive in all eighty-eight children. Clinical manifestations were present in twenty; in four there were skin lesions; in six visceral lesions; three had a marked epiphysitis; five had interstitial keratitis and one child was partially deaf. Twelve children received two courses or more of neo-arsphenamin and mercury intramuscularly; thirty-five have had one course; thirty have had less than one course; eleven failed to report for treatment.

Clinically all visible lesions yielded promptly to treatment.

Serologically, the Wassermann blood reaction is negative in fourteen; in twenty it is still + + + +. The reaction of several of these had been negative but it became positive again because of failure to continue treatment; in three cases the reaction is + + +, in two, + +, and in one, +. The remainder have not been examined since treatment was begun. (We have omitted from this series a number of older children whose reactions have become negative after intravenous treatment with arsphenamin combined with mercury intramuscularly.)

In fifty-nine cases, infection was denied by one or both parents, but two fathers admitted gonorrhea. In twenty-nine fathers, a history of syphilis was obtained. The age of the infection in these varied from 2 to 15 years. The number of years the parents had been married ranged from one to sixteen. Thirty-three fathers gave a strongly positive Wassermann reaction; thirteen a negative; forty-two we were unable to examine. Seventy-four mothers gave a strongly positive reaction; two a negative. In twelve we could secure no data as they were either dead or divorced. Fifteen mothers gave a history of miscarriages or stillbirths; sixty-one gave no such history; in the case of twelve mothers we could obtain no data. Thirty-one mothers had had no other children; in twenty-six cases, the other children all gave negative Wassermann reactions; in thirteen all gave positive reactions, and in eighteen both negative and positive. Eight of these women had had only partial antenatal treatment with arsphenamin and mercury; seven had had internal treatment only; sixty-one had had none, and twelve we could learn nothing about.

CONCLUSIONS

1. Every prospective mother should receive a routine Wassermann examination.

2. The proper treatment of a syphilitic mother during pregnancy will undoubtedly result in the birth of a healthy infant.

3. Every infant born of a mother or father with syphilis should have a Wassermann test made at birth; again two weeks later, then every four weeks up to six months, and after that every three months up to two years. If the reaction is negative with all these tests and no clinical signs have appeared, the baby has in all probability escaped the infection.

4. A certain number of infants born of mothers with strongly positive reactions give a positive cord reaction, but subsequently all tests are negative, and they fail to show any clinical manifestations of the infection. They should, however, be kept under observation for at least two years.

5. Occasionally an infant with active clinical signs of syphilis will give negative serologic findings, usually only temporarily. The clinical diagnosis should always take the precedence over the laboratory diagnosis and proper treatment should be instituted.

6. In the treatment of our patients having congenital syphilis we have adopted as the method of choice the systematic intramuscular injection of neo-arsphenamin and mercury. We not only have had good clinical results but we also have been able to obtain negative reactions in fourteen of our infants out of a total of forty-seven with ++++ blood reactions, when the treatment was begun within the first few months. This to our minds proves that systematic treatment begun early, in the first week or two where possible, will result in the clinical and serologic cure of the infant.

ABSTRACT OF DISCUSSION

Dr. William Allen Pusey, Chicago: I would like to express my great appreciation of this paper. I have gotten in a state of mind where I almost hate to hear a paper read which takes up the treatment of syphilis, because so many things are given as established facts that violate my clinical conceptions of what happens and has happened in syphilis. I was gratified to find that this paper did not in any way violate the conceptions that a good many of us have gathered after seeing the disease through many years.

On the subject of prenatal and postnatal treatment, it seems to me the paper represents very good end-rseults. It is a much better experience than we formerly had, and one which I am ready to believe is entirely within the facts.

Dr. Richard L. Sutton, Kansas City, Mo.: I, too, wish to express my appreciation of this excellent paper. The use of arsphenamin and neo-arsphenamin by intramuscular injection has always appealed to me, and when the drugs are properly administered by this route, I consider it far superior to the intravenous method.

Dr. Harold N. Cole, Cleveland: I have not obtained as good results in the prenatal treatment. I have had women in the hospital for the entire period of time and have given thorough treatment, but I have had a great many

babies that within two or three months would again show evidence of the disease. I have had no single ++++ Wassermann reactions, but have found mucous patches, and so on, and have been somewhat discouraged as to curing them.

In treating the babies, we use neo-arsphenamin and give it intravenously. By employing a fine pointed needle, we have no difficulty at all in administering a dose of 0.1 c. c. per kilogram. It is marvelous what will happen in the case of some of the babies that are about to die. In some cases, the injection of neo-arsphenamin into the vein will, within twenty-four hours, make an altogether different baby. There is no question that you can do much with neo-arsphenamin in the case of congenitally syphilitic babies that is impossible with mercury alone.

Dr. Jay Frank Schamberg, Philadelphia: The observation made by Drs. Fordyce and Rosen that children born of syphilitic parents may give a positive Wassermann reaction from the umbilical cord blood which may subsequently become negative is of considerable importance, because I am sure that the average physician would be likely to interpret such a finding at the time of birth as definite evidence of syphilis. On the other hand, I think it is the experience of many of us that children born of known syphilitic parents, and who exhibit negative reactions at birth, may commonly develop within two or three years positive Wassermann reactions or other evidences of syphilis; these evidences may not be the classic manifestations of the disease, but they may merely show a persistent anemia or a persistent subnormal weight which will not be overcome by anything except syphilitic treatment. I cannot but believe that such patients harbor spirochetes. I am sure that there are throughout the country tens of thousands of persons who have congenital syphilis which is entirely unsuspected, and I should like to emphasize the point that we must not regard the offspring of syphilitic parents as free of syphilis because of a negative Wassermann reaction at birth or even during the first year. I have seen such children subsequently develop symptoms that have yielded only to antisyphilitic treatment.

Dr. John A. Fordyce, New York: To answer Dr. Sutton's question, as to why we use neo-arsphenamin instead of arsphenamin, our reason is that it is less painful to the children. The method was devised at the clinic because of the ineffective methods of treating congenital syphilis, very inefficient mercury rubs usually being employed in these cases. Our results with the new method I think have proved that it is easily applied and is certainly efficient in curing a larger percentage than the older methods. It has been used in the Babies' Hospital by Dr. McLean, and in other institutions, and all have been much pleased with the results. It is much less dangerous than the intravenous method or that of introducing the solution into the longitudinal sinus. With the latter accidents occur, unless the work is in skilled hands.

I agree with Dr. Schamberg that there are many children going about who are syphilitic and who are harboring spirochetes. When they are cured, we cannot tell. Our work is too recent to permit the expression of any dogmatic opinion, but we hope it will be taken up by other members of the Association.

Dr. William Allen Pusey, Chicago: How much more painful are the injections than those of mercuric chlorid?

Dr. Isadore Rosen, New York: In reply to Dr. Pusey's question as to whether the babies have much pain: The babies cry while being treated but stop a few

minutes after they are returned to their mothers and apparently seem comfortable. We have given neo-arsphenamin intramuscularly to adults for the purpose of determining the amount of pain. They compare the pain to that of an ordinary intramuscular injection of mercury.

To answer Dr. Cole with regard to the treatment through the longitudinal sinus: I have seen photographs of pathologic specimens of brains (in the laboratory of Dr. Johnson of the Sloane Hospital) showing the results of treatment through the longitudinal sinus. There was a diffuse infiltration of the cortex with the drug, probably caused by some unavoidable accident during injection.

At the present time there are six institutions in New York City that have organized clinics for the treatment of congenital syphilis along the lines outlined by Dr. Fordyce and myself, and we hope in the near future to hear their reports.

THE TREATMENT OF SYPHILIS BY MERCURY INHALATIONS

HISTORY, METHOD AND RESULTS *

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AND
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HISTORY

Fumigations in the treatment of disease have been used since the time of Hippocrates. They were highly recommended by Celsus, Galen and others. Probably one of their first uses was in the treatment of scabies; therefore, it was only natural, when the skin manifestations of the new disease syphilis appeared in Europe that fumigations should have been mentioned as being employed to treat it. According to Astruc, to whose admirable book [1] we are indebted for much of our information regarding syphilis in early times, fumigations were first used in the treatment of syphilis by Angelo Bolognino, professor of surgery at the University of Bologna, in 1506. Jacques Catanee [2] also used them about the same time. Massa [2] speaks of them in his book on the treatment of the "Malady of Naples." Later, Matthiole,[2] in 1535, recommends them; likewise Fracastor, in 1546; Gabriel Fallopius, in 1560, in his book on "Mal Francois," and many others. William Rondelet,[2] in his book on the "Malady of Naples," reports "having cured by means of the fumigation of mercury a syphilitic ulcer on the nose which neither the Italian doctors nor those of Montpellier had been able to cure."

Fumigations as employed at first really combined fumigation and inhalation, but some of the later methods excluded inhalation; so that the methods may be discussed under two heads, the old type of treatment and the new type of treatment. With the old treatment, the patient, quite naked, was placed in a closed, heated chamber, in which were volatilized mercury compounds such as cinnabar, calomel, red

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* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

1. Astruc, Jean: Traité des Maladies Vénériennes, Paris, Cavelier and Sons **2**:177, 1754.

2. Quoted by Astruc (Footnote 1).

precipitate or turpeth mineral, often mixed with fats, resins, fragrant volatile oils, etc., to give off a dense smoke. The patient was exposed for from one-half to one hour, the treatment being given every day or so, depending on the patient's strength. Schiro [3] describes the typical inhalation rooms, such as those at Campailla and Modica in Sicily, as made of wood, thickly plastered, with a capacity of about 700 cubic meters, and having a small door. They were heated to 150 C. with a charcoal brasier, the patient was placed on a chair, and on the brasier was put 2 gm. of the heated sulphid of mercury and 1 gm. of incense. The door was then shut and treatment given for fifteen minutes, ten treatments making a course. He claims that the results were rapid; that the treatment was favorable to the patient in that he took no mercury by mouth; that it was harmless—a statement which we will take up later; that it did not interfere with the occupation; that there was a favorable diaphoresis, and that the treatment continued its effects for many months. He quotes Dr. Marendino, who found mercury seven months afterwards in the urine of a patient who had taken twenty inhalations and fumigations.

The so-called new treatment with fumigation was devised in 1776 by Lalouette [4] by the use of his "fumigation box." With this type the head was excluded entirely, and only pure calomel employed, which he claimed was not so irritating. As it is the scope of this paper to discuss rather the subject of inhalations, we shall not dwell further on Lalouette's method, except to mention Fournier's objections: 1. That it caused stomatitis and general debility if used too frequently. 2. That the dosage was uncertain. 3. That it was impracticable except in hospitals.

As concerns the old method of mercury inhalations, in which the head also was exposed to the vapors, there is no question that mercurial effects may be produced; but there can also be no question that the indefinite dosage makes the method either inefficient, or more often dangerous. This doubtless led to the abandonment of these inhalations. However, the lesson seems to have been forgotten, for these treatments are again advertised, as if they were new discoveries. A few citations from the literature should be useful for placing this matter in proper perspective.

LITERATURE

Astruc [1] reports the celebrated test of mercury inhalations as compared with mercury inunctions which was given before the city fathers and the faculty of medicine in the city of Paris, in 1733. His con-

3. Schiro, S.: New Orleans M. & S. J., November, 1909, pp. 62-65, 349-357.

4. Quoted by Fournier, A.: Treatment and Prophylaxis of Syphilis, English Translation, New York, Marshall Rebman & Co., 1906.

clusions were that, for the thirty-seven cases of syphilis—all of them of a more or less mild type—which were treated with the mercury inhalations, the treatment took as much time as would be recognized for the mercury inunctions. Moreover, four of the patients died during the course of the treatment—one of them as early as the ninth inhalation. Twelve of the patients, about one third, seemed to be benefited at the time by the fumigations, but later some of them showed signs of recurrence of the disease. He concluded that mercury inhalations should never be used on old people, on weak or debilitated individuals, on asthmatics or on people affected with any lung trouble. Fallopius [2] states that the therapy is advisable only for vigorous individuals, as he had had some bad results even with such picked cases.

Since mercury volatilizes somewhat even at ordinary temperature, and of course more rapidly when heated, accidental and industrial poisoning by mercury vapor is not uncommon, and sometimes occurs on a wholesale scale. These incidents illustrate toxic effects that may also follow therapeutic inhalation, since it is as impossible to control the dosage in the one case as in the other.

In 1810, the British ship "Triumph" had some mercury containers broken in its hold.[5] As a result, 200 sailors showed mercury poisoning and three of them died. All the birds and cattle on board the boat died. In 1804, as the result of a fire in a mine in India, a considerable amount of mercury was volatilized. Hermann [6] says "Nearly all the townspeople showed effects of mercury, though in slighter degrees than the miners, by contact with these, whose clothing was impregnated with mercury and giving off mercury vapor in the air. Even the animals, for instance, cows that pastured near the furnaces or in their lea, were affected. The cows became salivated, cachectic, and aborted, or the calves born at term died early." Nine hundred persons in the neighborhood had mercury tremors. Wherry [7] quotes Christison, who mentions two barometer makers who slept with their pot of quicksilver on the stove. One of them was slightly salivated and the other made tremulous for life. Seydel is quoted by Brouardel [8] as reporting the case of a woman who inhaled the vapor of mercury thrown on glowing charcoal. After one or two minutes, she fell unconscious and, although no more mercury was inhaled, died in ten days with typical acute mercury poisoning. Merget is quoted by the same author as finding all the air from the floor to the ceiling in a mirror factory to contain mercury. A. Gautier is quoted by the same author as reporting the circumstance of

5. Binz: Pharmakologie, Ed. 2, 1891.
6. Hermann, L.: Wien med. Wchnschr., 1850, No. 40.
7. Wherry, G.: The Practitioner **51**:168, 1893.
8. Brouardel, P.: Les Intoxications, 1904, p. 247.

some men who, having vaporized 200 gm. of mercury in a room, not entirely closed, become ill, one dying after a few days. Binz mentions two cases of poisoning from the presence of poorly silvered mirrors in the room. It is not necessary to adduce further examples of the tragic accidents following inhalations of mercury vapor in human subjects; but it is interesting to remark in passing that A. Krogh ("The Respiratory Exchange of Animals and Man") warns specifically against the use of any mercury in closed-space respiration apparatus.

Systematic investigations of the effects of mercury vapor have been made on animals, with important results. It is easy to produce mercury poisoning in this manner. In this country, for example, Schamberg, Kolmer and Raiziss [9] showed that a rabbit may show effects of mercury by being exposed to the vapor of mercury arising from a second rabbit inuncted with mercurial ointment. Similar experiments were reported by Wile and Elliott.[10] A series of excellent experiments was made by von Baerensprung [11] in 1850. Rabbits exposed for from one quarter to one hour to the vapor of boiling mercury died within a few days. Another rabbit kept in a cage with an open dish of mercury, at room temperature, became ill in two weeks, and died in the third week. All rabbits showed considerable irritation of the air passages and lungs; small hyperemic areas, and some areas of consolidation. In one of the rabbits that had been exposed to boiling mercury, droplets of mercury were found in these consolidated areas. Eulenberg [12] also found marked congestion of the mucosa, from the trachea to the smallest bronchi, in rabbits that died as the result of exposure to mercury vapor.

Binz cites the statements of Kirchgaesser, 1865, Samelsohn, 1872, and Fr. Mueller, 1806, that rabbits, when exposed to the vapor of mercury ointment in a closed, warm space, die after stomatitis and considerable swelling of the salivary glands. Merget [12] exposed animals to amalgamated copper plates. Death occurred sooner in warm weather than in cold. Small animals were more susceptible than large, young more than old. He found no changes in the lungs. Solles [13] found birds much more susceptible than rats. The symptoms were mainly nervous. Skudro [12] exposed mice to the vapor from gray ointment. Death occurred after one or several days. The principal lesions consisted of acute hemorrhagic inflammation of the lungs; the kidneys also showed

9. Schamberg, J. F., Kolmer, J. A., and Raiziss, G. W.: Absorption of Mercury, J. A. M. A. **70**:142 (Jan. 19) 1918.

10. Wile, U. J., and Elliott, J. A.: Absorption of Mercury, J. A. M. A. **68**:1024 (April 7) 1917.

11. Von Baerensprung: J. f. prakt. Chem. **50**:21.

12. Quoted by Ricker and Hesse: Arch. f. path. Anat. **217**:267-307, 1914.

13. Solles: Bull. Soc. d'anat. et physiol. de Bordeaux **2**:20-32, 1881.

degeneration. Pulmonary lesions occurred when mice were killed by inunction, in which inhalation also played a part, but not when inhalation was avoided by oral or hypodermic administration.

Important experimental comparisons of inhalation and other methods of administration were made by Ricker and Hesse.[14] For inhalation, the animals were placed in cages with the opening half closed by linen cloth coated with gray ointment, arranged so that it could not be touched by the animals. The principal lesions were found in the lungs: hyperemia, with or without hemorrhage, and sometimes inflammation (pus cells). The lesions started as small, isolated areas, which fused as they extended. Inflammatory changes were often present also in the kidneys and colon.

With other methods of administration, the pulmonary changes were smaller, those of the kidneys and intestine greater. The pulmonary congestion is, therefore, mainly a local reaction to the inhalation.

SUMMARY OF THE LITERATURE

In summarizing the experimental literature, it is seen that the inhalation of mercury vapor, either by exposure for short periods to heated mercury or by longer periods to ointment, etc., at room temperature, produced all the ordinary phenomena of all grades of mercury poisoning, and, in addition, inflammatory changes in the air passages and lungs. A similar condition doubtless exists in human cases. For instance, Binz [15] points out that, of the crew of the "Triumph," four men, who had been well previously, died from phthisis soon after the accident. A fifth, who had recovered from the mercury, died of pneumonia.

It may be remarked, in passing, that the possibility of producing mercurial effects from the vapors arising from the ointment has led to some curious methods of administration, such as Merget's "mercurial flannels" and Blaschko's "mercolint." These were made by soaking the fabric first in a bichlorid solution and then in a solution of ammonia. The mercury was thus precipitated in the form of a fine gray powder on the cloth. This cloth was then enveloped in lint and placed in a pillow or around the neck. It was claimed that this would give off sufficient vapor of the metal to produce the desired therapeutic effect.[16] Merget,[17] and Blaschko even go as far as to assert that in mercury inunctions the entire effect is due to inhalation of mercurial vapor that is volatilized from the skin. In like manner, Thalmann has suggested

14. Ricker and Hesse: Arch. f. path. Anat. **217**:267-307, 1914.
15. Footnote 5, p. 491.
16. Footnote 4, p. 94.
17. Quoted by Fournier, A. (Footnote 4, p. 80).

the use of unguentum hydrargyri placed inside the nose and Cromquist [18] the use of snuffing gray powder. The same principle is used in "mercuriel," an amalgam of mercury, aluminium and magnesium. It is a dry powder, suspended in a bag on back or chest, and intended to give off mercurial vapor, which is supposed to be inhaled. Poulsson [19] states that the clinical results are much feebler than with inunction. The fundamental error in all this type of attempted continuous inhalation is that they do not sufficiently confine the air that the patient breathes. They could be successful only if the patient sojourned continuously in a small cabinet.

THE THEORETICAL FOUNDATION OF INHALATION THERAPY

The advocates of inhalation methods must concede the very serious disadvantages of indefinite dosage, which they have made no serious effort to correct. To offset this, they must assume that the lung is a good absorbing surface for mercury; that inhalation prevents local contact with the digestive tract; and that irritation of the pulmonary system is less objectionable than irritation of the intestines. None of these assumptions is well founded; indeed, each is contrary to fact.

The assumption as to prompt pulmonary absorption was based on analogy with the absorption of gases. The analogy, however, does not hold, since only soluble gases could pass through the endothelium. The fallacy was pointed out by Hermann,[20] in 1874: "In the case of the inhalation of mercury vapors, there is no doubt that the metal is deposited as such, in fine droplets, on the mucosae of the respiratory and digestive tracts. Even though it were demonstrated experimentally that these may penetrate into the blood and lymph vessels . . . they would probably be oxidized before they could act . . . It is much more probable that the deposits of very finely divided metal on the mucosae are oxidized before absorption . . . It is a false physical conception that mercury vapors could be absorbed as such into the blood, through the lungs; when vapors pass a moist surface, they must be condensed there; and it is this condensed condition which comes in question for absorption." Fürbringer [21] believes that mercury vapors, on coming into contact with the moist mucous membranes, are deposited as metallic mercury. It could not be taken up as metallic mercury until after it had been dissolved in the surface. In other words, absorption would occur, but would not be faster nor essentially different from that in any other mucous membrane.

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18. Cromquist, C.: Arch. f. Dermat. u. Syph. **86**:180-196, 1907.
19. Poulsson: Lehrbuch der Pharmakologie, Horvel, Leipzig, 1912.
20. Hermann, L.: Lehrbuch der experimenteller Toxicologie, 1874, p. 212.
21. Fürbinger, P.: Arch. f. path. Anat. **82**:491, 1880.

The second assumption, that inhalation would avoid the local effects on the digestive tract, is incorrect because a considerable part of the mercurial vapor is condensed on the mucous membranes of the mouth and pharynx and is gradually swallowed with the saliva. The proportion that thus goes into the digestive tract doubtless varies with conditions; but it must be considerable, and may well be the major part. Certainly in the patients treated by Thalman and Cromquist, with their so-called "Schnupfungkur," much of the drug would be swallowed and absorbed through the digestive tract.

Finally, the seriousness of pulmonary injury is sufficiently illustrated by the experimental data. Nor is there any question of choice between pulmonary and intestinal effects, since inhalations are liable to produce both.

THERAPEUTIC METHODS AND OPINIONS

From the foregoing considerations, it would be expected that the inhalation or fumigation methods would be undesirable; it is difficult to conceive any real advantage over even the oral method of administration; while the uncertain dosage would be liable to make the treatment either inefficient or dangerous, the dangers being enhanced by the possibility of pulmonary irritation. By arranging the treatments so that only a small amount is actually inhaled, and most of the mercury goes innocuously into the air, the danger may be greatly reduced; and, by repeating such small treatments sufficiently often, an adequate dosage might finally be obtained; or by more audacious procedures, a more prompt action might be attainable, with corresponding and uncontrollable risk. In one or the other of these ways, inhalations could be used if they were the only available methods of administering mercury; but the uncertainty and risk would appear to compare unfavorably with the oral methods of administration.

It should not be forgotten that fumigations received a quite thorough clinical trial at one time, but were found unable to compete, in the long run, with other methods. Since the experience of one generation is so easily lost to the next, it may be worth while to quote the details of the methods formerly in vogue. Wood [22] says, "The vapor when inhaled operates more rapidly than any other form in which mercury is used and has, therefore, been recommended in cases in which a very speedy effect is required, the impression being afterward sustained by the internal use of the medicine." However, he is then careful to go on to say that he has personally never met with a case in which it seemed to be desirable! and also to say that violent effects are said sometimes

22. Wood: Therapeutics, Ed. 1, 1856 **2**:277.

to have resulted from the inhalation of the vapor. Different forms of the drug were employed and recommended. Mr. Abernethy [23] employed the black oxid but this was especially for the true mercury fumigations: "The patient, being protected by a complete suit of underclothing, was placed at night in a vapor bath with the head projecting and the neck guarded by a cloth, and exposed for fifteen to twenty minutes to the vapor of two grams of the oxid put on a heated iron within the bath." He was then transferred to bed and passed the night in the same garments. Wood said salivation was possible by this method in forty-eight hours. Cinnabar,[24] has likewise been used, and to give the best effects the vapor must be inhaled. In using cinnabar, sulphurous acid would be inhaled at the same time, rendering the compound very unpleasant and even hazardous. From 10 grains to 1 dram was employed. In the past, calomel has likewise been used and is supposed to have caused less inflammation.

Calomel vapor was also applied directly to local lesions. Kans [25] devised an apparatus consisting of a bulb glass tube ending in a fine point. The bulb was heated in order that the calomel would vaporize, and a current of air was passed through the tube and the point was then directed against the skin lesion which he desired to treat.

CLINICAL EXPERIMENTS ON MERCURY INHALATION

Although neither the theoretical consideration nor the published experimental or clinical data appeared promising, it seemed worth while to investigate as to whether the method could be sufficiently improved to make it available for the occasional cases in which other methods might be undesirable. The obvious improvements could be made in two directions; to minimize the inaccuracies of dosage; and to select the least irritant preparation. The greatest inaccuracy in the existing methods lies in the fact that the mercurial vapor goes into the air without any control as to how much or little enters the mouth. This source of inaccuracy was avoided by placing a weighed quantity of the mercury compound in the center of a strong glass tube, about 10 inches long, bent to an angle of about 130 degrees, and open at both ends. The mercury was then volatilized by heating lightly in a Bunsen flame, the patient inhaling the vapor as it was formed, by deep inhalations from the end of the tube. Calomel could be volatilized directly in this manner. Metallic mercury, however, presented some practical difficulties. These were overcome by using a 10 per cent. trituration with chalk, and by heating this in the corked tube, depositing the

23. Quoted by Wood (Footnote 22, p. 287).

24. Footnote 22, p. 304.

25. Quoted by White, Hale: Textbook of Pharmacology and Therapeutics, 1901, p. 435.

mercury as a mirror on the walls. The chalk could then be emptied, and the mirror easily volatilized by heat at the time of the treatment.

This method insures the actual inhalation of a perfectly definite dosage, a point that has not been met by any previous method. Nor was any significant amount of mercury reexhaled, since the vapor condenses very rapidly in the mouth. How much of the vapor was deposited in the mouth, how much entered the trachea, and how little entered the bronchioles, we have no means of knowing.

The second object of selecting the least irritant preparation was also fairly accomplished. Metallic mercury was much less irritant than calomel; and it seems very improbable that any of its compounds could be less irritant than the metal itself.

DOSAGE

In selecting the dosage, we could not be guided by the doses employed in the older methods in which only a fraction enters the mouth. On the contrary, if the absorption of the mercury were really efficient, the dosage should rather be that used in intramuscular injections. Should this dosage be inefficient, then inhalation would evidently have no advantage, so far as absorption is concerned. On the other hand, increasing the dosage beyond this point would present two dangers: on the one hand, the fact that variable absorption might produce toxic systemic effects; on the other hand, the susceptibility of the lungs to local injury.

Calomel inhalations were begun according to the following schema:

COURSE I

The patient was given the first course consisting of:

First day, 5 mg. of calomel
Second day, 10 mg. of calomel
Third day, 20 mg. of calomel
Fourth day, 20 mg. of calomel
Total, 75 mg. of calomel
Fifth, sixth and seventh days, no medication.

COURSE II

The patient was then given the second course consisting of:

First day, 10 mg. of calomel
Second day, 20 mg. of calomel
Third day, 40 mg. of calomel
Fourth day, 80 mg. of calomel
Total, 150 mg. of calomel.

We were careful not to use this treatment on any patient who was having symptoms of bronchial irritation or who was under treatment

with iodids or bromids. We also watched carefully for symptoms of bronchial and pulmonary irritability, albumin in the urine and salivation. Especial symptoms will be noted on each patient as observed.

This dosage was devised to lead up to the usual intramuscular dosage of calomel; i. e., about 200 mg. per week. However, the occurrence of local irritation made it inadvisable to increase the dosage further, so we turned to metallic mercury.

Brief abstracts of the clinical observations follow.

CASE 1.—C., a man, white, aged 31, with a diagnosis of secondary syphilis and having a maculopapular eruption, with patches in mouth, gave a ++++ blood Wassermann reaction. The spinal fluid was negative. The teeth in good condition.

COURSE I

First day, 5 mg.; observation negative.

Second day, 10 mg.; slight bronchial irritation during and fifteen minutes after inhalation.

Third day, 20 mg.; observation same as on second day.

Fourth day, 40 mg.; slight amount of salivation during inhalation, and bronchial irritation during, and twenty minutes after, inhalation.

Three days vacation intervened.

COURSE II

First day, 20 mg.; observations negative.

Second day, 40 mg.; patient coughed a few times during inhalation.

Third day, 60 mg.; slight bronchial irritation during, and ten minutes after, inhalation.

Fourth day, 80 mg.; observations same as third day.

Final Examination.—The urine was normal throughout the experiment. The gums and teeth were negative, there was no salivation, and the lungs were negative. At no time was there an improvement in the syphilitic condition. However, these symptoms cleared up nicely under arsphenamin and mercury inunctions.

CASE 2.—K., aged 26, presented a condition which was diagnosed as maculopapular syphilid. The blood Wassermann reaction was ++++; the spinal fluid negative.

COURSE I

First day, 5 mg., observations negative.

Second day, 10 mg., slight bronchial irritation during inhalation.

Third day, 20 mg., bronchial irritation during, and fifteen minutes after, inhalation.

Fourth day, 40 mg., slight salivation and bronchial irritation during, and twenty-five minutes after, inhalation.

Fifth, sixth and seventh days, no medication.

COURSE II

Eighth day, 10 mg., slight bronchial irritation during inhalation.

Ninth day, 20 mg., slight salivation and bronchial irritation during, and bronchial irritation for twenty minutes after, inhalation.

Tenth day, 40 mg., increased salivation and bronchial irritation during, and bronchial irritation for thirty minutes after, inhalation.

Eleventh day, 80 mg., profuse salivation during, and bronchial irritation for thirty minutes after, inhalation.

After the inhalation on the tenth day, the patient complained that his gums were getting sore and bleeding easily when brushed.

Final Examination.—The gums were edematous and there was an increased amount of saliva at end of course. The syphilis showed no evidence of improvement. The urine was negative as to albumin throughout the experiment. The syphilitic lesions disappeared rapidly on use of arsphenamin and inunctions.

CASE 3.—M., a man, aged 23, presented a condition which was diagnosed as secondary syphilis, with a maculopapular syphilid. The blood Wassermann reaction was ++++; the spinal fluid negative.

COURSE I

First day, 5 mg., observations negative.

Second day, 10 mg., slight bronchial irritation during inhalation.

Third day, 20 mg., bronchial irritation during, and fifteen minutes after, inhalation.

Fourth day, 40 mg., slight salivation and bronchial irritation during, and twenty-five minutes after, inhalation.

Fifth, sixth and seventh days, no medication.

COURSE II

Eighth day, 10 mg., slight bronchial irritation during inhalation.

Ninth day, 20 mg., slight salivation and bronchial irritation during, and bronchial irritation for twenty minutes after, inhalation.

Tenth day, 40 mg., increased salivation and bronchial irritation during, and bronchial irritation for thirty minutes after, inhalation.

Eleventh day, 80 mg., profuse salivation during, and bronchial irritation for thirty minutes after, inhalation.

After the inhalation on the tenth day the patient complained that his gums were getting sore and bleeding easily when brushed.

Final Examination.—The gums were edematous and there was an increased amount of saliva at the end of the course. The syphilis showed no evidence of improvement. The urine was negative as to albumin throughout the experiment. Syphilitic lesions disappeared rapidly on use of arsphenamin and inunctions.

CASE 4.—M., a man, aged 23, whose condition was diagnosed as secondary syphilis, with maculopapular eruption, patches in mouth and primary lesion on glands, gave a blood Wassermann reaction which was ++++. The spinal fluid was negative.

COURSE I

First day, 5 mg., observations negative.

Second day, 10 mg., tickling sensation in throat and coughing a few times during inhalation.

Third day, 20 mg., observations same as on second day.

Fourth day, 40 mg., patient complained of sore throat, coughing a few times, and slight salivation during the latter part of inhalation.

COURSE II

Eighth day, 10 mg., observations negative.

Ninth day, 20 mg., slight bronchial irritation during, and ten minutes after, inhalation.

Tenth day, 40 mg., patient complained of tender teeth and gums, increased bronchial irritation during, slight salivation and coughing for thirty minutes after, inhalation; gums edematous.

Eleventh day, 80 mg., patient noticed the dosage was increasing because he was coughing more than after other inhalations. Increased salivation during, and for ten minutes after inhalation, together with coughing for thirty minutes thereafter.

Final Examination.—After the last inhalation, an examination revealed edematous gums and an increased amount of saliva. There was no improvement in the syphilitic symptoms; the urine showed no albumin. The eruption and mucous patches healed rapidly after the use of arsphenamin.

CASE 5.—C., a man, aged 32, with a diagnosis of maculopapular syphilid of a generalized type, gave a blood Wassermann reaction of ++++. The spinal fluid was negative.

COURSE I

First day, 5 mg., observations negative.

Second day, 10 mg., patient noticed tickling sensation in throat, coughing twice during inhalation.

Third day, 20 mg., patient noticed increased amount of saliva, bronchial irritation during, and twenty minutes after, inhalation. No salivation after inhalation.

Fourth day, 40 mg., profuse salivation and bronchial irritation during and fifteen minutes after inhalation. Examination after inhalation revealed edematous gums and an increased amount of saliva.

Fifth, sixth and seventh days, no medication.

Eighth day, 20 mg., slight bronchial irritation during, and for fifteen minutes after inhalation.

Ninth day, 40 mg., profuse salivation and bronchial irritation during, and fifteen minutes after, inhalation.

Tenth day, 60 mg., observations same as day previous, gums and teeth not sore.

Eleventh day, 80 mg., profuse salivation and bronchial irritation during, and for twenty-four hours after, inhalation.

Final Examination.—This revealed edematous gums and an increased amount of saliva. The lungs eight hours after inhalation showed signs of a bronchitis. The temperature varied from 99 F. after the fourth inhalation to 103 F. after the eighth. Two days after the last inhalation, the temperature returned to normal. The syphilitic condition showed no improvement; the urine remained normal as to albumin throughout the experiment. The syphilitic lesions reacted at once when arsphenamin and mercury rubs were used.

SUMMARY OF OBSERVATIONS ON CALOMEL INHALATIONS

Inhalations of from 5 to 80 mg., totaling 225 mg. in two weeks, were taken by each of five patients, with active syphilitic lesions. None of these showed any therapeutic response, nor any renal changes. All but one exhibited definite bronchial irritation, salivation, and tenderness or edema of the gums. The bronchial irritation and salivation occurred at

the time of each inhalation, and were evidently due to direct local contact with the calomel, and not to systemic action. This probably holds true also of the irritation of the gums. In brief, then, calomel inhalation produced no systemic effects, therapeutic or toxic; but it caused local irritation, increasing with the dosage, that made further increase of dosage inadvisable, especially in view of the case, reported by Henry Lee,[26] of a young woman who, after breathing calomel vapor, became unconscious, livid and cyanosed, death ensuing. Necropsy showed the lungs to be congested, but the other organs healthy. This brings to mind also the four patients, reported by Astruc, who died while undergoing inhalation experiments.

INHALATION OF METALLIC MERCURY

The mercury was deposited as a mirror in the tubes, so that it could be readily volatilized. The following courses were administered, with the same precautions that were described under calomel.

First day, 5 mg. mercury
Second day, 10 mg. mercury
Third day, 20 mg. mercury.
Fourth day, 40 mg. mercury (two inhalations of 20 mg. each)
Total in week, 75 mg. mercury
Fifth, sixth and seventh days, no medication.

COURSE II

First day, 10 mg. mercury
Second day, 20 mg. mercury
Third day, 40 mg. mercury (two inhalations of 20 mg. each)
Fourth day, 80 mg. mercury (four inhalations of 20 mg. each)
Total in week, 150 mg. mercury
Fifth, sixth and seventh days, no medication.

Course III was added after experience had shown that Courses I and II did not produce either local or systemic effects.

Accepting the weekly dose for mercury by intramuscular injection as about 140 mg., this is equaled by the second course, and doubled by the third course of inhalation.

Abstracts of the clinical histories follow.

CASE 6.—R., colored, aged 25, single, with a diagnosis of secondary syphilis, presenting a generalized papular and annular syphilid. Laboratory findings were: Blood Wassermann reaction, ++++; spinal fluid negative.

The patient received inhalations as specified in the first two courses without noticing any objective or subjective bronchial symptoms or symptoms of mercurialism. The patient received arsphenamin injections (six) while receiving the inhalations.

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26. Quoted by Fournier, Footnote 4, p. 93.

CASE 7.—C., white, single, aged 25, presented a condition which was diagnosed as secondary syphilis, with lesion on the glans penis, a generalized papular syphilid and condylomata lata. The laboratory findings were: Blood Wassermann reaction, ++++; spinal fluid negative.

The patient received the first two courses of inhalations as specified without noticing any subjective or objective bronchial symptoms or symptoms of mercurialism. The patient received arsphenamin injections (six) while receiving inhalations.

CASE 8.—W., white, single, aged 38, gave a diagnosis of secondary syphilis, with maculopapular eruption, mucous patches in the mouth, and condylomata lata around the anus. The blood Wassermann was ++++; the spinal fluid negative.

This patient was started with the second course of inhalation and without a vacation given the third course. As far as the eruption was concerned there was very little change; the lesions were not as bright in color, but they increased in number. In addition, between the second and third inhalations of the second course the patient developed mucous patches in his mouth. The inhalations did not especially irritate him. The urine showed no albumin during the course of the treatment. The lesions cleared rapidly on use of arsphenamin and mercury inunctions thereafter.

CASE 9.—B., colored aged 29, gave a diagnosis of rupoid syphilid, generalized in type. The blood Wassermann was ++++; the spinal fluid negative.

This patient received the second course of inhalations as specified in outline, three days vacation, and two inhalations of the third course. During the inhalations there was no change in the lesions, the teeth and gums were negative, the temperature was generally normal in the morning, rising to around 38.6 in the afternoon. There was no bronchial irritation. The patient complained of a sore throat which continued until arsphenamin was given. Examination showed no mucous patches. The inhalations were not continued because the patient was getting worse and running a temperature. After 0.5 gm. arsphenamin was given, the temperature became normal and the patient improved almost at once. The urine remained normal throughout the treatment.

CASE 10.—Q., white, aged 26, gave a diagnosis of secondary syphilis, generalized maculopapular in type. The blood Wassermann was ++++; the spinal fluid negative.

The patient received the course of inhalation as specified in the outline. After three inhalations (Course I) the patient developed two mucous patches on the hard palate, the eruption remaining about the same. The observations were negative during the second course. During the third course the eruption faded a little, and after the fourth inhalation of Course III the patient noted a transitory salivation. No bronchial irritation was noted. Patient received no other therapy except the routine mouth washes. The lesions all cleared up rapidly thereafter with arsphenamin. The urine was normal throughout the treatment.

CASE 11.—C., white, aged 38, with a condition diagnosed as generalized macular eruption, primary on the glans, gave a blood Wassermann reaction ++++. The spinal fluid was negative.

The patient received the courses, 1, 2 and 3 of inhalations, as specified above, without noticing any especial objective or subjective symptoms. There was no change in the character of the lesions, the patient developed no mucous patches, and experienced no bronchial irritation, or salivation. He complained of a frontal headache on admittance which continued until arsphenamin was

administered at the end of Course III. During the three courses of inhalations the patient received no other therapy except the routine mouth washes. The syphilitic lesions then reacted at once to arsphenamin.

SUMMARY OF METALLIC MERCURY INHALATIONS

Inhalations of from 5 to 160 mg. of mercury, to a total of from 225 mg. in two weeks to 750 mg. in three weeks, were administered to each of six patients. No systemic or local effects resulted; no salivation (except in one doubtful case) and no sore gums. The weekly dosage amounted to from two to five times the customary intramuscular dosage. It is evident that the absorption must be materially smaller than with intramuscular injections.

CONCLUSIONS

Inhalations and fumigations of mercury have been tried at various times, since the earliest days of the appearance of syphilis in Europe. They have always been abandoned as of uncertain efficiency, and occasional high toxicity. None of the methods so far proposed contain essential improvements over these antiquated methods.

The unsatisfactory results are due mainly to the uncertain dosage. Local injury to the lungs is an additional factor.

The assumption that mercury would be more promptly absorbed by the lungs was based on physical misconceptions. In fact, the mercury is condensed on the mucous membranes of the mouth, pharynx, and respiratory tract. That in the mouth and pharynx is, for the most part, swallowed. The absorption then takes place by the gradual conversion of the mercury into soluble compounds, just as it does with the ordinary administration of "gray powder."

An improved technic was devised to insure the complete inhalation of definite doses of mercury or calomel, equivalent to these used in intramuscular injection. This was applied by a series of patients with active syphilis, but without any therapeutic or other systemic response. Larger doses appeared unjustifiable. Calomel produced objectional local irritation.

The results indicate that the administration of mercury compounds by inhalation has no advantage over oral administration; but, on the contrary, it has the serious disadvantage of indefinite dosage, and the consequent difficulty of steering between inefficiency and danger, and of special danger of respiratory irritation.

ABSTRACT OF DISCUSSION

Dr. August Ravogli, Cincinnati: When I had the service in the hospital, I used inhalations of calomel. I had a cabinet made with a chair and under the chair was placed an alcohol lamp with some water and, in the middle, 15 grains of calomel. The water began to boil and carried with the vapor

the particles of calomel. I can say I have found just what Dr. Cole says: the method is unreliable for we do not know the absorbed quantity of calomel, and the patients get weak and begin to suffer right away with stomatitis, gingivitis and so on. The fumigation with mercury I have not tried, but I do not think it is to be recommended.

Dr. William Allen Pusey, Chicago: Dr. Cole has the disagreeable habit of asking in connection with popular practice, "What happens when you do this thing?" Then he goes ahead and shows us. Last year he read a very enlightening paper on the absorption of mercury injections and this year he gives us an excellent paper on this inadequate method. It is very important to have this information. The paper is also timely, because a preparation of this sort is being put out at present. The manufacturers have added frankincense and myrrh or something of that sort to the mercury and are giving us fumigation again.

ERYTHEMA NODOSUM SYPHILITICUM *

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The prime purpose of this paper is to direct the attention of dermatologists to a subject that has received scant consideration during the last fifteen years; a subject which seems to be not fully understood at the present time, and which is worthy of painstaking study, namely: the relation of syphilis to erythema nodosum. The scarcity of research contributions to the literature on this subject in recent years is due in part to the rare occurrence of the combination, and in part to a failure seemingly to appreciate the importance of the relationship. The latter attitude is entirely explicable. The term "erythema nodosum syphiliticum" implies that syphilis may be an independent cause of what is known clinically as erythema nodosum. Unfortunately the term has been applied loosely, without due consideration of its true meaning, to cases in which more than mere association was not proved; and this fact, together with the really great difficulty of determining a true causal relationship, has led many to doubt the validity of the whole conception. Nevertheless, since the fundamental papers on erythema nodosum syphiliticum were written the organism of syphilis has been discovered, the doctrine of focal infection has been elaborated, a better understanding of embolism and thrombosis as affecting the skin prevails, and the bacterial origin of simple erythema nodosum has been established. The subject therefore is ripe for investigation by every dermatologist; and those who have an abundance of dermatologic and syphilitic material at their command are particularly fortunate in the opportunity before them.

The puzzling elements in a case combining the features of erythema nodosum and syphilis are shown in the following clinical report:

REPORT OF A CASE

Mrs. X, a vigorous appearing woman of 35, married and living with her husband, presented herself complaining of "sore lumps" on her legs, which had been present about a week. Examination showed a number of deep-seated, slightly elevated lesions on the anterior and lateral surfaces of the legs below the knee; these were from 1 to 3 cm. in diameter, rather intensely red in color, firm in consistency, with no signs of deep fluctuation, and distinctly tender. There had been no initial chill; her temperature was normal, and she had not at any time been conscious of having fever. There was some joint dis-

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

comfort; the throat was red but not particularly sore; the tonsils were not enlarged. The condition was diagnosed as erythema nodosum, and the patient was placed on full doses of the salicylates. This medication was continued several weeks with a complete absence of therapeutic results. Further checks were put on the diagnosis. A biopsy was requested, but consent was not given. Efforts made to discover a systemic tuberculosis were fruitless; a Wassermann test, however, gave a +++ reaction. Acting on this finding, she was placed on mixed treatment; the success of this, as shown in the rapid melting away of the lesions, was as surprising as had been the previous failure to obtain relief with the salicylates. It was subsequently learned that an obscure illness from which her husband suffered was tabes complicated with tuberculosis. The patient, who had never been pregnant, could give no clue as to the time syphilis began; leaving out of consideration the lesions described, she presented nothing that would place her in the secondary stage. During the following year there was a recurrence of the lesions on the leg in a much milder degree, and there appeared on the lower part of the back a number of small gummas; both conditions were relieved with mixed treatment. To make the problem more puzzling, three years after the original experience, she passed through what seems to have been an attack of erythema nodosum; she had sore throat, enlarged tonsils, decided rheumatic pains and typical lesions on the legs—this condition developing during a period in which her Wassermann reactions were negative, and being relieved by salicylates.

Was the original attack in this case an erythema nodosum syphiliticum, as indicated by its prompt response to mixed treatment and its resistance to the salicylates? Or was it a combination of both syphilitic and rheumatic elements in which the former predominated? While the former diagnosis seemed at first to be certain, subsequent developments in the case pointed to the presence of a combined etiology.

LITERATURE ON ERYTHEMA NODOSUM SYPHILITICUM BETWEEN 1880 AND 1905

To show, however, that the conception of erythema nodosum syphiliticum is fundamentally sound I would direct attention briefly to certain basic contributions which appeared during the period between 1880 and 1905, and which, presented chronologically, not only show the steps in the evolution of the idea but also point the direction which future investigations will take.

The term erythema nodosum syphiliticum originated with Mauriac who published his observations on "Early Syphilitic Affections of the Subcutaneous Cellular Tissue" in 1880 and 1881.[1] The lesions coming under this general head he classifies into three groups, namely: (*a*) erythema nodosum syphiliticum; (*b*) early neoplasms, circumscribed and resolutive; and (*c*) early neoplasms, circumscribed and ulcerative. His description of the condition designated erythema nodosum syphiliticum is essentially as follows: It occurs in relatively

1. Mauriac, Charles: Ann. de dermat. et syph. **1**:419, 1880; **2**:471, 1881.

severe syphilis four or five months after infection and is acute in onset; the lesions are found predominantly on the legs below the knees but may appear elsewhere; they consist of round and oval nodosities and hypertrophic plaques irregularly distributed throughout the subcutaneous tissue; some are free, some are more or less adherent to the overlying skin; dependent on their size and their degree of adherence, the lesions may show elevation, and the overlying skin may vary in color from normal to a deep violaceous and ecchymotic hue; in severe cases the skin may have a swollen, shiny, edematous appearance. There is usually some spontaneous pain and always marked tenderness on pressure. In the process of resolution the adherent plaques and nodules gradually lose their attachment to the skin, becoming free before their disappearance. The lesions of the second group develop insidiously without accompanying symptoms, are indolent in course, and tend to disappear by absorption with or without preliminary softening. The third group of lesions, however, break down quickly and form ulcers.

Sixteen years later de Beurmann and Claude,[2] under the title "Erythema Nodosum of Syphilitic Origin" confirmed in a series of cases the observations of Mauriac, and presented these conclusions: There may be found, in the course of syphilis, cutaneous manifestations which duplicate with absolute fidelity the clinical type erythema nodosum. The pathogenesis of these lesions is in dispute, and while they may be due to an infection added to the syphilis, they are more often due to the syphilis itself. Further, there exists between erythema nodosum syphiliticum and gumma of the subcutaneous tissues a series of intermediate stages which establish a transition from one to the other, and which indicates that the difference between the two is merely one of intensity of the pathologic process.

Thus it is seen that de Beurmann and Claude unite the three classes of Mauriac and make them all a part of the same process.

In 1900 Phillipson,[3] in an article on "Embolism and Metastasis in the Skin," reviewed a previous work of his in which he had been able to show that the beginning of a subcutaneous gumma had been in an endophlebitis obliterans. He had later repeated this finding in serial sections of a subcutaneous nodule taken from a syphilitic patient with lesions much resembling those of erythema nodosum. Phillipson contends that all erythemas are hematogenous in origin, arising from metastasis and thrombosis; that these vascular changes are found much more frequently in veins than in arteries; and that phlebitides are often found in the deeper layers of the cutis and subcutaneous tissue where they appear clinically as deep-seated nodules. Thus Phillipson

2. De Beurmann and Claude: Ann. de dermat. et syph. **27**:485, 1896.
3. Phillipson: Arch. f. dermat. u. syph. **51**:33, 1900.

shows the relationship of erythema nodosum-like gummas and phlebitis, and offers an explanation of the pathogenesis of the lesions of Mauriac and de Beurmann and Claude.

In 1902, appeared the work of Max Marcuse[4] on "Nodular Syphilis and Syphilitic Phlebitis." He reported three cases of secondary syphilis of severe type, in which there appeared on the legs below the knees lesions more or less suggestive of erythema nodosum. In one in which the lesions showed no signs of breaking down, the resemblance was most exact; in another, while the early lesions became ulcerative, the later ones preserved their resemblance to erythema nodosum completely; in a third, three types of eruption were present: discharging furuncle-like lesions, softening gumma-like nodes and hard, erythema nodosum-like nodules; all of these he regarded as expressions of the same process. Further, in this third case he was able to establish, by a careful histologic examination of serial sections, the presence of a phlebitis and periphlebitis developing into a partially necrobiotic granulation tumor with the essential characters of a gumma. He concludes that these lesions resembling erythema nodosum which appear in early syphilis should be regarded as specific; that they may or may not break down; and that they originate in the walls of the subcutaneous veins and present some analogies to certain forms of nodular tuberculosis.

Thus Marcuse shows also the connection between erythema nodosum syphiliticum and phlebitis, and confirms Phillipson's view of the pathogenesis of Mauriac's nodular lesions.

In 1905, E. Hoffmann,[5] in an extensive contribution on "Diseases of the Veins in Secondary Syphilis," reviews the entire literature of his subject and reports additional cases. He divides the phlebitides of secondary syphilis into three groups: (*a*) strand-like phlebitis, (*b*) nodular periphlebitis, so-called "nodose syphilid," and (*c*) erythema nodosum syphiliticum and erythema multiforme syphiliticum. It is impossible to discuss all the applicable points to be found in this valuable paper. A few may be mentioned briefly. He would apply the term "nodose syphilid" to the bullet and spindle-shaped nodules which develop in the subcutaneous tissues of the leg shortly after the first exanthem, usually in women with varicose veins; these lesions may or may not break down, and they start from the vein walls, especially from those sclerosed by varicosity. Erythema nodosum syphiliticum occurs most commonly in women with fresh syphilis; it begins acutely, resembles simple erythema nodosum closely, and resolves promptly under specific treatment without breaking down. In a typical case he

4. Marcuse, Max: Arch. f. dermat. u. syph. **63**:3, 1902.
5. Hoffmann, Erich: Arch. f. dermat. u. syph. **73**:38 and 245, 1905.

was able to show that the condition started with a phlebitis of a small subcutaneous vein: He regards erythema multiforme syphiliticum as an involvement of veins more superficially placed, namely, those of the cutaneous network. Thus Hoffmann further confirms the findings of Phillipson and Marcuse.

COMMENT

The authorities mentioned are not all that have made contributions of value to the subject; they suffice to show, however, that from Mauriac to Hoffmann, a period of twenty-five years, erythema nodosum syphiliticum passed from a proposed recognition as a clinical expression of syphilis to a fairly definite establishment on anatomic grounds as a syphilitic process. The three groups of Mauriac have been shown to be stages of the same process; that process has been demonstrated to be essentially gummatous; and these gummatous changes have been found to have their inception in the walls of the veins. All of this, too, has occurred before the discovery of *Spirochaeta pallida,* now known as an organism incessantly attacking the walls of the vascular channels, and before the working out of the pathogenesis of simple or rheumatic erythema nodosum, now shown to be an embolic process. The intensive study of further cases, in the light of knowledge already acquired, ought to settle the status of erythema nodosum syphiliticum beyond question. But with such final settlement new problems will arise, for if syphilis is accepted as an independent producer of the lesions of erythema nodosum, then, in the interest of consistency and clarity in dermatology, our conception of erythema nodosum must be revised and the nomenclature we are applying must be readapted. Other infective agents than those of rheumatism and syphilis must be conceded a rôle in the etiology; and the simple term erythema nodosum, without a modifying word showing etiology, will stand for a symptom only and not for a disease entity. Lastly, as tuberculosis is a bacillary systemic infection, and as many cases of associated tuberculosis and erythema nodosum have been observed, it is quite possible that a new chapter will need to be written on that condition which resembles erythema nodosum in so many respects, namely, the erythema induratum of Bazin.

ABSTRACT OF DISCUSSION

DR. SIGMUND POLLITZER, New York: I would like to lay special emphasis on the point that erythema nodosum should not be looked on as a disease but as a symptom, bearing in mind that it is, moreover, a symptom of a great many underlying conditions, in all of which there occurs an endophlebitis of embolic origin. With this general conception clearly in mind, it is evident that a syphilitic may present an endophlebitis due to streptococcus or staphylococcus infection. We know that these lesions occur in tuberculosis; I believe it was

Landouzy who first found tubercle bacilli in these lesions and from their tissue made successful inoculations in guinea-pigs. We are sure today that *Spirochaeta pallida* is also capable of producing these lesions. I believe that attention was first drawn to the possibility of erythema nodosum being syphilitic because a disproportionately large number of cases of erythema nodosum was observed in syphilitic clinics as compared with those seen in the ordinary dermatologic clinics. It is not possible to recognize the cause of the disease from the appearance of the lesions, and it is entirely possible for a syphilitic patient to have a tuberculous or a rheumatic erythema nodosum. I presume the only possible way of differentiating in the syphilitic patient would be to apply the clinical test, because the biopsies in these cases practically always show the same kind of lesions, namely, an endophlebitis.

The therapeutic deduction to be drawn from the observations so well set forth by the reader of the paper is that in every case of erythema nodosum we should look for the possibility of syphilis.

DR. RICHARD L. SUTTON, Kansas City, Mo.: I have for a long time been convinced that erythema nodosum may be due to any one of several different causes. I will admit I never thought of syphilis, but since hearing Dr. McEwen's paper I am convinced that syphilis may be a cause. It may be due to infection with the streptococcus, the staphylococcus or the tubercle bacillus, and it may be due to certain anaphylatic processes. I usually look for an infection of the teeth or tonsils in association with erythema nodosum, and it is almost invariably present. In cases of this kind, while syphilis may predispose to the disorder, it gives us one more cause for the development of the symptom commonly known as erythema nodosum.

DR. ERNEST L. MCEWEN, Chicago (closing): My intention in reviewing the literature was not to consider anything subsequent to 1905, the date of the discovery of *Spirochaeta pallida;* Dr. Leviseur's article was published in 1911.

My purpose in presenting this paper was to stimulate investigation along this line. I think the more recent findings relative to erythema nodosum make it necessary to reconsider the entire subject. As we learn more about the different infections, we must be ready to alter our nomenclature if necessary.

I think Dr. Pollitzer has stated the idea clearly, and if my paper will stimulate dermatologists to make further investigation I shall feel that I have accomplished something.

THE EXCRETION OF ARSENIC AFTER SERIAL ADMINISTRATION OF ARSPHENAMIN AND NEO-ARSPHENAMIN *

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Clinically, it is of considerable importance to possess accurate knowledge relative to the period that such arsenical preparations as arsphenamin and neo-arsphenamin remain in the human body. At present little is known concerning this point except that arsenic leaves the body in the excretions, the elimination extending over a relatively long period after a single injection. Little or nothing is known concerning the length of time arsenic remains in the body or its rate of excretion when the organic arsenic preparations before mentioned are administered in repeated doses. It is conceivable that study of the excretion of arsenic under these circumstances may give a better conception of the action of these compounds and lead to improvement of the method of treatment. It is possible, for instance, that under repeated injections the tissues of the organism become more or less saturated with the arsenical compound and that the excess is merely eliminated without having served any useful purpose. Under these circumstances one may assume that smaller doses in the later period of administration would be just as efficacious as the initial larger dose, and hence diminish the probability of any detrimental effect which the arsenic itself may initiate. It was with this point of view in mind that the present investigation was begun, the details of which are herewith presented.

HISTORICAL

P. Usuelli [1] found that after the intravenous injection of arsphenamin, excretion of arsenic in the urine began within two or three hours and continued for a period of ten or twelve days. He stated also that arsenic was found in small quantities in the feces and was vomited four days after injection of the arsphenamin.

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* From the Department of Pharmacology and Toxicology, Yale University.

* The data are taken from the thesis presented by Stanton H. Davis in partial fulfilment of the requirements for the degree of M.D., Yale University, 1920.

1. Usuelli, P.: Elimination of Arsenic by Patients Treated with "606," Internat. Kong. Syphilog. Dermatol. **7** (April) 1912.

Merkuriev [2] asserts that the quantity of arsenic present in the urine after arsphenamin injection is not constant and that the period of excretion is of longer duration after intravenous injection than it is when the drug is administered intramuscularly.

Karl Ullmann [3] demonstrated that the excretion of arsenic was greatest on the first day subsequent to intravenous injection of arsphenamin and that the elimination decreased rapidly thereafter.

After intramuscular administration of arsphenamin, Muto and Sanno [4] demonstrated that the urinary excretion of arsenic reached a maximum of 12 or 13 per cent. in from four to six days. Nearly 66 per cent. of the arsenic was eliminated in the first eight days, 5 or 6 per cent. being excreted the eighth day. Traces of arsenic were still present in the urine the twentieth day.

Irokawa [5] recovered from 40 to 90 per cent. of the arsenic administered as arsphenamin, and states that the excretion is slow after intravenous injection. During the first day, 10 per cent. of the arsenic injected was recovered, the greater part within a week, although a small portion was still being eliminated at the end of three weeks.

The work of Bornstein [6] on subcutaneous injections and of Zimmern [7] on concentration of dosage gives similar results, but it will be observed that in every instance the investigation was concerned with arsenic excretion after single injections only.

EXPERIMENTAL

As has been stated previously, the present communication is concerned with the study of the excretion of arsenic after the administration of arsphenamin and neo-arsphenamin in series doses, as given in ordinary practice.

Subjects of the Experiment.—Subject 1: A patient in the medical service of the New Haven Hospital, had been under a course of treatment with arsphenamin since August, 1919, but for seven weeks he had been receiving potassium iodid without arsenic preparations.

2. Merkuriev, V. A.: Arsenic in Urine After Injection of Arsphenamin, Russk. Vrach. **11**:989-990, 1912.

3. Ullmann, Karl: Excretion and Retention of Arsphenamin, Arch. f. Dermat. u. Syph. **114**:511.

4. Muto, K., and Sanno, Y.: Elimination of Arsenic After Intravenous Injection of Arsphenamin, Therap. Monatsh. **25**:599-601.

5. Irokawa, K.: Excretion of Arsenic in Urine After Subcutaneous or Intramuscular Injection of Arsphenamin, Sei-i-Kwai M. J. **33**:59 (Oct.) 1914; abstr., J. A. M. A. **63**:2077 (Dec. 5) 1914.

6. Bornstein, A.: Fate of Arsphenamin in the Body, Deutsch. med. Wchnschr. **37**:112.

7. Zimmern, F.: Infusion or Injection of Arsphenamin, München. med. Wchnschr. **60**:1087.

Twenty-four-hour specimens of urine and feces were collected daily, from Feb. 1, 1920, to March 15, 1920. February 4, he received 0.6 gm. arsphenamin intravenously, and thereafter the same dose every seven days, until a total of six injections had been reached.

Subject 2: A patient in the medical service of the New Haven Hospital, with an aortic aneurysm diagnosed as of syphilitic origin, received injections of neo-arsphenamin as given in Table 1.

TABLE 1.—ADMINISTRATION OF NEO-ARSPHENAMIN (SUBJECT 2)

Date of Injection	Dosage	Date of Injection	Dosage
3/24/20	0.15 gm.	4/14/20	0.15 gm.
3/30/20	0.15 gm.	4/19/20	0.15 gm.
4/ 4/20	0.15 gm.	4/24/20	0.2 gm.
4/ 9/20	0.15 gm.	4/29/20	0.2 gm.

The analysis of the urine and feces in this case was begun April 17, after the patient had received five doses of 0.15 gm. of neo-arsphenamin each. After the sixth injection of 0.15 gm. of neo-arsphenamin, the dose was raised to 0.2 gm. The patient was discharged May 3, and further study became impossible.

Method of Arsenic Determination.—The method used for quantitating the amount of arsenic present was that of the Gutzeit reactions as modified by Sanger and Black.[8]

THE EXCRETION OF ARSENIC AFTER REPEATED INJECTIONS OF ARSPHENAMIN AND NEO-ARSPHENAMIN

In Tables 2, 3, 4 and 5, and in Charts 1, 2, 3 and 4 may be found data obtained relative to this investigation. The graphic representation of the excretion brings out much more clearly, perhaps, the salient features. In the first case after the first injection, the largest urinary excretion of arsenic occurred on the day of administration and gradually decreased on subsequent days. Less than 1 per cent. of the injected arsenic was eliminated through the urine previous to the second injection. After the second injection and also subsequent to the following injections, there was a rise in excretion on the day of injection, but the maximum excretion occurred on the day after injection. This second-day rise was increasingly larger with each injection except the third. After the rise on the second day the excretion fell off rapidly until the next dose, but in each subsequent week it maintained a higher daily average excretion than the week previous. In brief, each injection caused a higher second-day rise and higher daily average excretion than the one preceeding it, and the longer the injections were con-

8. Sanger and Black: The Quantitative Determination of Arsenic by the Gutzeit Method, Proc. Am. Acad. Arts & Sc. **43**:8 (Oct.) 1907.

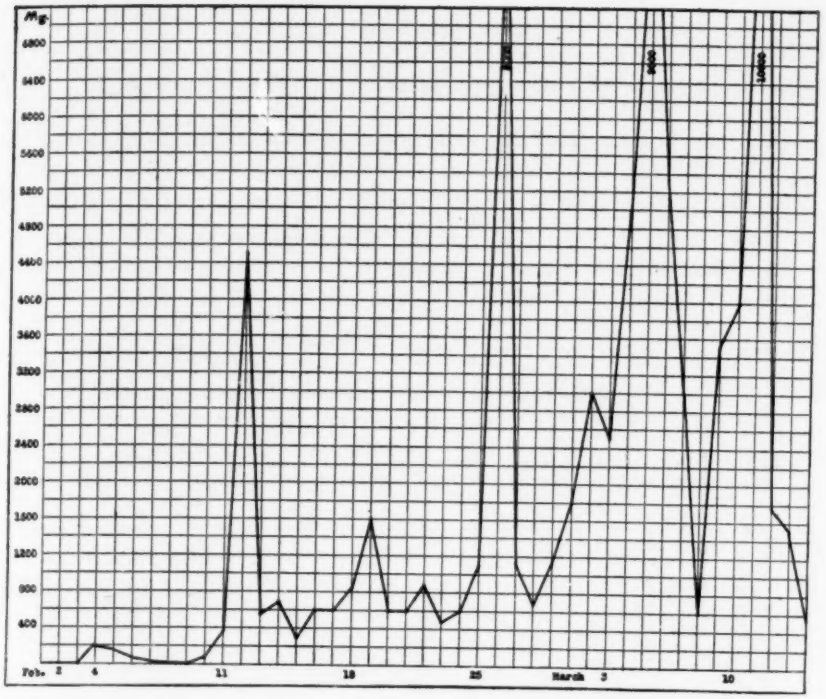

Chart 1 (Subject 1).—The urinary excretion of arsenic after serial intravenous administration of arsphenamin.

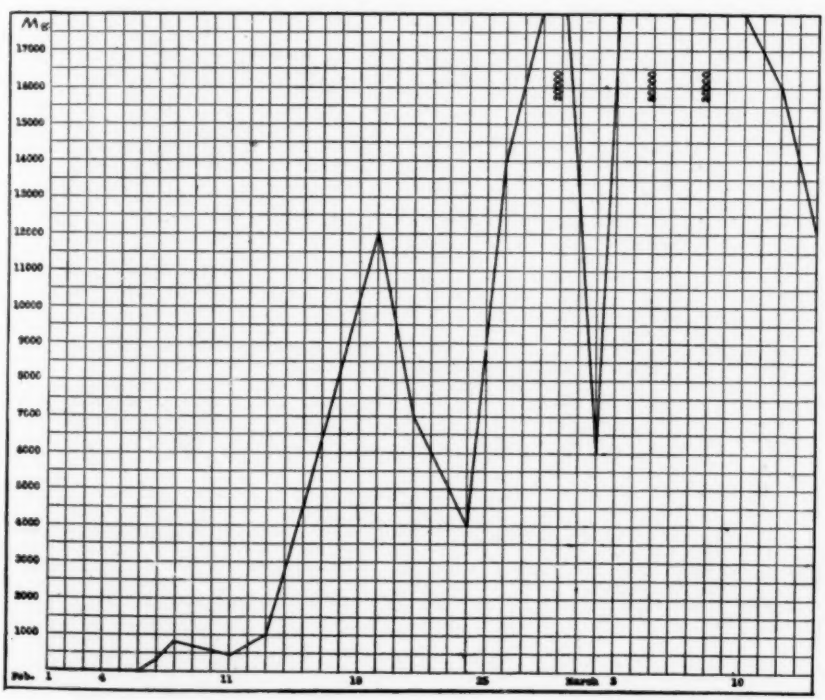

Chart 2 (Subject 1).—The excretion of arsenic in the feces after serial intravenous administration of arsphenamin.

tinued the greater was the percentage of the arsenic excreted in the interval before the next injection.

The same result was found in an even more marked degree in the second case with neo-arsphenamin. In this case, however, the effect of the first injection could not be studied, as the patient had already received several injections before the analyses were started.

TABLE 2.—The Urinary Excretion of Arsenic After Serial Intravenous Administration of Arsphenamin (Subject 1)

Date, 1920	Volume, C.c.	Total Arsenic, Mg.	Percentage of Previous Injection	Total Excretion in per Cent. of Total Injections	Injections of Arsphenamin
2/ 2	1,470	None	—		
2/ 3	450	None	—		
2/ 4	660	200	0.1	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/ 5	1,140	150	0.08		
2/ 6	390	50	0.03		
2/ 7	690	30	0.02		
2/ 8	426	10	0.005		
2/ 9	1,050	None	—		
2/10	1,110	75	0.04	0.275	
2/11	1,210	375	0.2	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/12	720	4,500	2.42		
2/13	630	550	0.29		
2/14	690	700	0.37		
2/15	840	300	0.16		
2/16	660	600	0.32		
2/17	1,190	600	0.32	4.08	
2/18	2,460	875	0.47	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/19	480	1,600	0.86		
2/20	1,410	600	0.32		
2/21	1,140	600	0.32		
2/22	1,090	900	0.48		
2/23	1,200	450	0.24		
2/24	1,314	600	0.32	3.01	
2/25	1,450	1,100	0.59	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/26	630	8,000	4.30		
2/27	940	1,125	0.60		
2/28	1,320	675	0.36		
2/29	170	1,125	0.60		
3/ 1	1,158	1,800	0.96		
3/ 2	1,158	3,000	1.61	9.02	
3/ 3	800	2,500	1.34	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
3/ 4	930	5,000	2.69		
3/ 5	990	9,000	4.84		
3/ 6	1,050	5,350	2.88		
3/ 7	1,080	3,000	1.61		
3/ 8	780	600	0.32		
3/ 9	580	3,500	1.88	13.68	
3/10	630	4,000	2.15	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
3/11	780	10,000	5.38		
3/12	360	1,750	0.99		
3/13	480	1,500	0.81		
3/14	480	500	0.26	11.47	

In the analyses of the stools of Subject 1 no arsenic was found until the third day after the first injection. From that time on there was a general rise, which was most marked about two or three days after the various injections. After the second injection, and continuing on through the whole series, the greater part of the arsenic excreted came through the gastro-intestinal route

The analyses of the stools of Subject 2 reveal the same results in regard to the extent of time between the injection and maximum excretion, but in this case, in which smaller doses were used (0.15 and 0.2 gm. of neo-arsphenamin), the percentage of excretion in the feces was not so large in proportion to that in the urine, with the exception of the second injection interval.

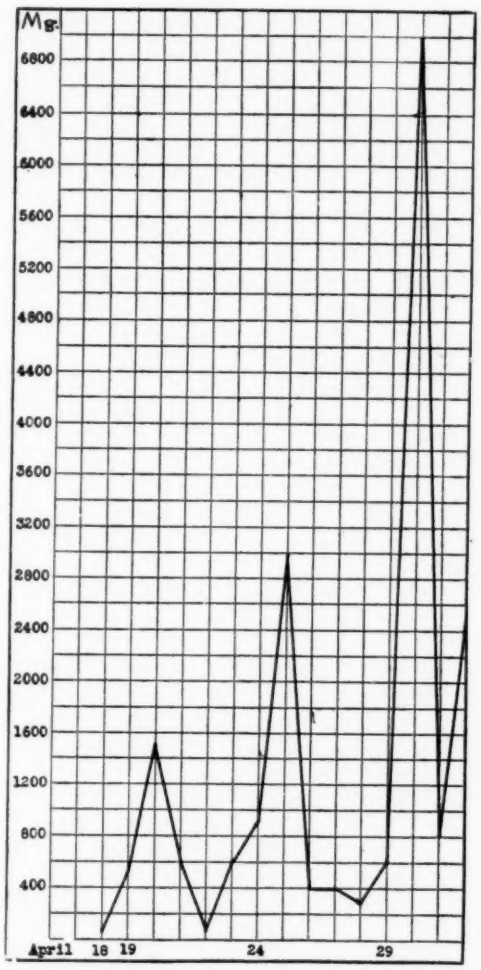

Chart 3 (Subject 2).—The urinary excretion of arsenic after serial intravenous administration of neo-arsphenamin.

These results seem to demonstrate that, although arsenic is slow in appearing in the intestinal content, in a series of intravenous injections of arsphenamin or neo-arsphenamin the greater part of the arsenic is excreted by that route. No attempt was made to localize the point of

TABLE 3.—The Excretion of Arsenic in the Feces After Serial Intravenous Administration of Arsphenamin (Subject 1)

Date, 1920	Moist Feces, Gm.	Total Arsenic, Mg.	Total Excretion in per Cent. of Total Injections	Injections of Arsphenamin
2/ 2	250.8	None		
2/ 3	184.5	None		
2/ 5	110.4	None	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/ 6	26.0	None		
2/ 7	95.5	300		
2/ 8	192.0	800	0.59	
2/11	26.0	300	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/12	52.0	150		
2/13	355.0	1,000		
2/15	593.0	4,500	3.19	
2/19	114.0	12,000	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/21	126.6	7,000		
2/24	333.0	4,000	12.36	
2/26	104.0	14,000	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
2/29	251.0	20,000		
3/ 2	400.0	6,000	21.51	
3/ 5	363.0	80,000	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
3/ 8	399.0	20,000	53.76	
3/12	173.0	16,000	.....	0.6 gm. arsphenamin = 186,000 mg. arsenic
3/13	76.0	14,000		
3/14	311.0	12,000	22.58	

TABLE 4.—The Urinary Excretion of Arsenic After Serial Intravenous Administration of Neo-Arsphenamin (Subject 2)

Date, 1920	Volume, C.c.	Total Arsenic, Mg.	Percentage of Previous Injection	Total Excretion in Per Cent. of Total Injections	Injections of Neo-arsphenamin
4/18	720	40	0.12	0.12	
4/19	860	500	1.51	.....	0.15 gm. neo-arsphenamin = 33,000 mg. arsenic
4/20	900	1,500	4.53		
4/21	600	600	1.82		
4/22	960	50	0.15		
4/23	1,560	600	1.82	9.83	
4/24	1,080	900	2.04	.....	0.2 gm. neo-arsphenamin = 44,000 mg. arsenic
4/25	1,080	3,000	6.82		
4/26	540	400	0.91		
4/27	750	400	0.91		
4/28	720	300	0.68	11.36	
4/29	660	600	1.36	.....	0.2 gm. neo-arsphenamin = 44,000 mg. arsenic
4/30	930	7,000	15.91		
5/ 1	920	800	1.82		
5/ 2	540	2,500	5.68	24.77	

TABLE 5.—THE EXCRETION OF ARSENIC IN THE FECES AFTER SERIAL INTRAVENOUS ADMINISTRATION OF NEO-ARSPHENAMIN (SUBJECT 2)

Date, 1920	Moist Feces, Gm.	Total Arsenic, Mg.	Total Excretion in per Cent. of Total Injections	Injections of Neo-arsphenamin
4/17	89.0	1,000	3.03	
4/19	114.0	1,250	.....	0.15 gm. neo-arsphenamin = 33,000 mg. arsenic
4/21	72.5	2,000		
4/22	189.0	10,000	40.14	
4/25	150.2	3,750	.....	0.2 gm. neo-arsphenamin = 44,000 mg. arsenic
4/26	129.7	6.000	21.92	
4/29	118.0	2,250	.....	0.2 gm. neo-arsphenamin = 44,000 mg. arsenic
5/ 2	120.5	8,500	24.34	

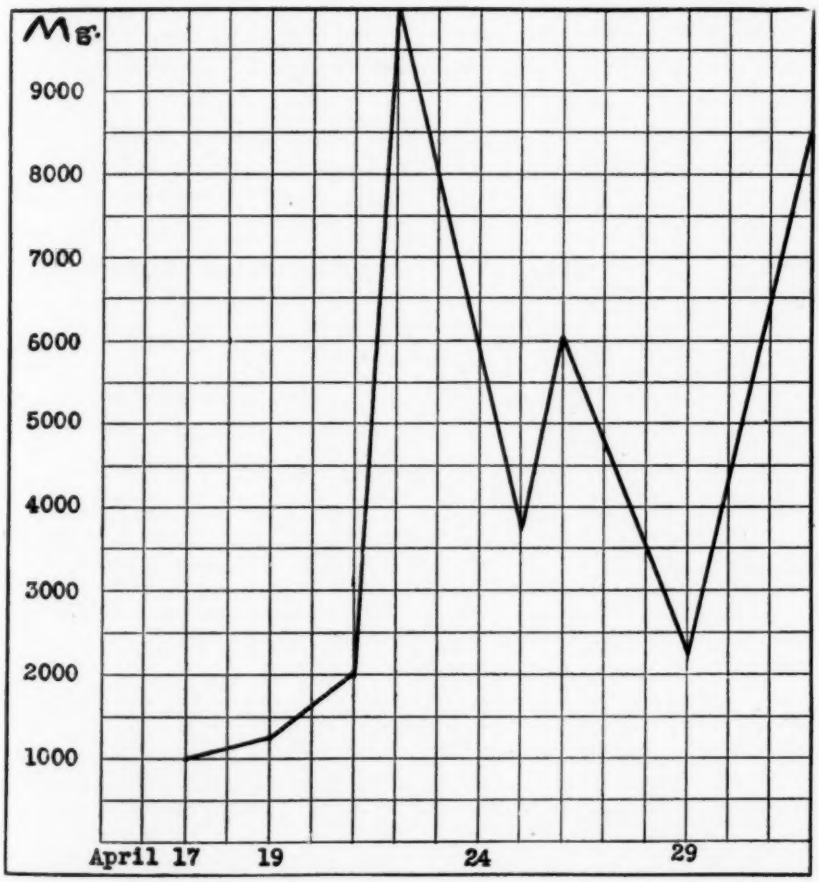

Chart 4 (Subject 2).—The excretion of arsenic in the feces after serial intravenous administration of neo-arsphenamin.

excretion, as to whether it was in the stomach, large or small intestine, or in an organ emptying into the gastro-intestinal canal. However, Bornstein [6] and Burnashev [9] have found that, after intravenous injection of arsphenamin, arsenic is deposited chiefly in the liver, kidneys and spleen. Therefore, it is conceivable that with the chief deposit of arsenic in the liver the probable source of arsenic in the feces would be through the bile. Incidentally, if this should be the case, the administration of cholagogues in arsenical poisoning would be a logical therapeutic measure.

For a better comparison of the relative excretions Table 6 and Chart 5 were prepared showing the percentage of excretion of the total arsenic injected. In the first case this shows a regular and rapid increase in the percentage of arsenic excreted following each injection. This holds true for the urine, feces and total excretion. In the second case, it must be borne in mind that the series is not complete and is therefore only comparable with the later injections in the first case. However, here the percentage of excretion does not show a regular rise, but varies between 30 and 50 per cent.

Throughout the analyses it is notable that there is no relation between the amount of either the urine or the feces and the quantity of arsenic excreted in them. The most satisfactory explanation of this is on the basis that the excretion rate is in proportion to the arsenic in the blood and that the eliminating organs would excrete in that proportion up to the limit of their capacity.

CONCLUSIONS

1. Arsenic appears in the urine within a few hours after intravenous injection of arsphenamin or neo-arsphenamin.

2. The maximum excretion occurs on the day of or the day after injection.

3. In a series of injections the maximum excretion is higher with each succeeding dose.

4. In a series of injections the percentage of arsenic excreted is small in the first interval in both urine and feces, and increases in each injection with each succeeding dose and interval.

5. Arsenic appears in the feces more slowly, but within three or four days after intravenous injection.

6. In a series of injections the total percentage of arsenic excreted in the feces is larger than in the urine, being as high as 53.76 per cent. in one week.

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9. Burnashev, A.: Fate of Arsphenamin in the Body, Russk. Vrach **13**:442, 1912.

TABLE 6.—THE PERCENTAGE EXCRETION OF ARSENIC AFTER SERIAL ARSPHENAMIN AND NEO-ARSPHENAMIN INJECTION

	Injection	Arsenic Injected, Mg.	Percentage Excreted in Urine	Percentage Excreted in Feces	Total per Cent. Excreted	Remarks
Subject 1	1	186,000	0.275	0.59	0.865	
	2	186,000	4.080	3.19	7.270	
	3	186,000	3.010	12.36	15.370	
	4	186,000	9.020	21.51	30.530	
	5	186,000	13.680	53.76	67.440	
	6	186,000	11.470	22.58	34.050	Incomplete
Subject 2	1	33,000	0.120	3.03	3.150	Incomplete
	2	33,000	9.830	40.14	49.970	
	3	44,000	11.360	21.92	33.280	
	4	44,000	24.770	24.34	49.110	

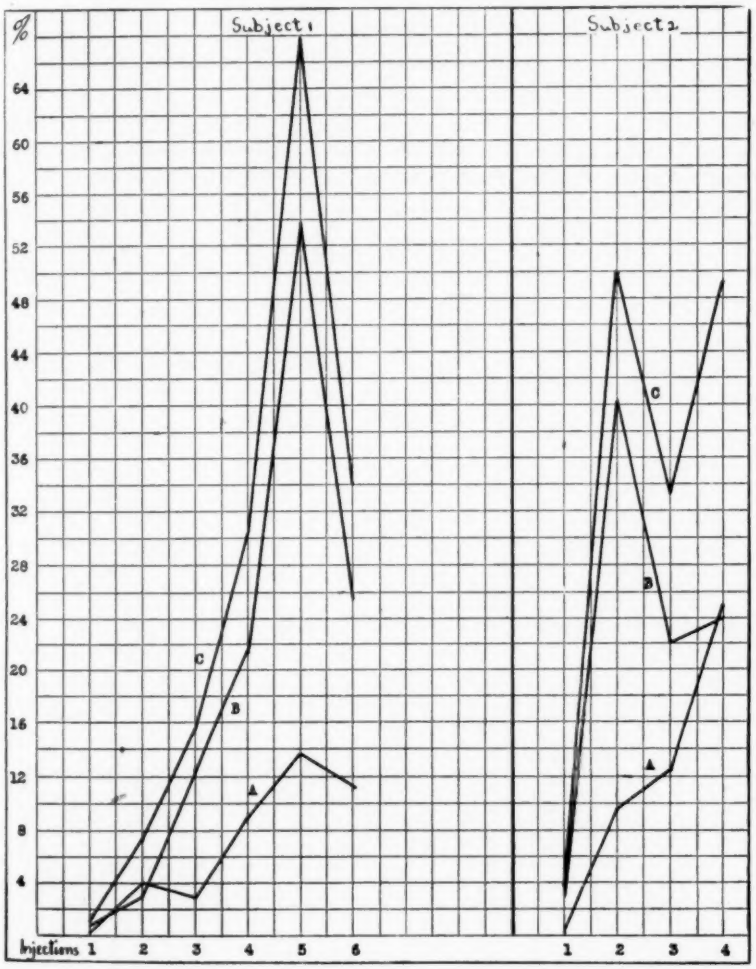

Chart 5.—The percentage excretion of arsenic after serial injections of arsphenamin and neo-arsphenamin. A, urine; B, feces; C, total.

7. There is no relation between the amount of arsenic excreted and the quantity of urine or feces.

8. These facts are interpreted to mean that, in the early intervals of the serial treatment with arsphenamin and neo-arsphenamin, the arsenic compounds are retained in the body up to a point at which the tissues are, as it were, saturated with them. When this point has been reached further additions of the arsenical preparations are in large measure quickly eliminated from the body.

9. If this interpretation is correct, it would seem logical to modify the serial treatment to the extent that smaller doses may be given when the point of saturation has been reached, unless indeed it is at this point that the initial beneficial influence is exerted.

10. Although further study is necessary before a positive conclusion may be drawn, it would appear that the point of saturation is attained at about the fourth injection.[10]

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10. In addition to the references given, the following will be found of interest: Gautier: Bulletin Soc. Chemique **24**:250. Chittenden and Donaldson: Am. Chem. J. **2**:235.

THE ELIMINATION OF ARSPHENAMIN AND NEO-ARSPHENAMIN IN THE URINE

A CHEMICAL AND CLINICAL STUDY OF THE ABELIN REACTION *

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The need for a simple, and at the same time accurate, means by which the elimination of arsphenamin and its derivatives can be studied in the urine is apparent. In a paper read before the Section on Dermatology and Syphilology of the Thirteenth International Medical Congress held at London in 1913, Vennin,[1] a French army surgeon, has well stated the case thus: "A survey of the elimination possesses an importance upon which it is not necessary to insist since we have seen what an important rôle renal impermeability plays in intoxication. The ideal method would be to follow by a simple reaction accessible to all physicians, the elimination of arsenobenzol [arsphenamin] in the urine. This is still another problem for study as yet unsolved."

THE CHEMICAL STUDY OF THE ABELIN REACTION

The elimination of arsphenamin and neo-arsphenamin in the urine has attracted little attention. Leredde and Rubinstein[2] of Paris consider the elimination of these drugs important and have referred to it in Leredde's last work on syphilis. Other investigators who have made studies of this substance qualitatively or quantitatively are: Abelin,[3]

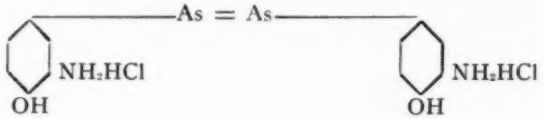
* From the laboratory of Physiological Chemistry of the University of Illinois, College of Medicine.

1. Vennin: Traitement de la Syphilis dans l'armée par le salvarsan et les substances alliées, Proc. Thirteenth International Med. Congress, 1913, Section 13, pp. 176-190.

2. Leredde and Rubinstein: See Leredde and Domaine: Traitment et prophylaxie de la syphilis, Ed. 2, Paris, Maloine et Fils, Editors, 1921, p. 320.

3. Abelin, J.: Ueber eine neue Methode das Salvarsan nachzuweisen, München. med. Wchnschr. **58**:1002, 1911. Ibid.: Beginn und Dauer der Ausscheidung Salvarsans durch den Urin nach intravenoeser Injektion, München. med. Wchnschr. **58**: 1771-1773.

Gaebel,[4] Lehmann,[5] Wilcox[6] and Webster.[7] The elimination of arsphenamin in the urine has been based on the qualitative and quantitative determination of arsenic by chemical methods and by the biologic method. The method devised by Abelin[8] based on a specific color reaction is the only exception and was used in our investigation, and also by Leredde and Rubinstein, Escallon,[8] Riebes,[9] Koetter[10] and Frankel-Heiden and Navassart.[11]



Chemistry of Arsphenamin and Its Derivatives.—(*a*) Arsphenamin is the hydrochlorid of 3-diamino-4-diphydroxy-1-arsenobenzene. Arsphenamin is prepared by nitration of paraphenyl arsenic acid with the subsequent reduction and condensation of the nitrophenyl arsenic acid.

(*b*) Neo-arsphenamin is sodium 3-diamino-4-dihydroxy-1-arsenobenzene-methanal-sulphoxylate with inert inorganic salts.

Neo-arsphenamin is prepared by precipitating a salt of 3-diamino-4-dihydroxy-1-arsenobenzene with sodium methanal sulphoxylate and dissolving the precipitate in alkalis. From the resultant solution neo-arsphenamin is obtained by the addition of alcohol or acetone.

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4. Gaebel, G. Otto: Das Salvarsan beim gerichtlichen Arsennachweis, Arch. d. Pharm. **249**:49-56, 241-247, 1911.

5. Lehmann, F.: Ueber die Bestimmung des Arsens in Salvarsan und Neosalvarsan, Apoth. Ztg. **27**:545-546, 1912.

6. Wilcox, W. H., and Webster, John: The Toxicology of Salvarsan, Brit. M. J. **1**:474, 1916.

7. Webster: Excretion and Secretion of Salvarsan and Neo-Salvarsan, Analyst, Lond. **41**:231-240, 1916.

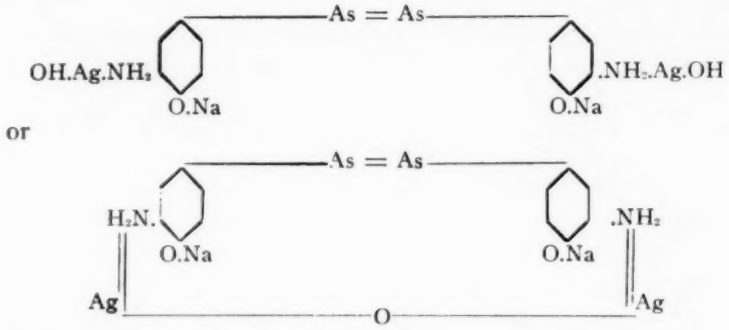
8. Escallon, J.: Sur l'elimination du 606 dans les urines, Lyon. méd. **119**: 377-383, 1912.

9. Riebes: Ueber die Verarbeitung des Salvarsans und Neosalvarsans im Organismus, Arch. f. Dermat. u. Syph., 1914, p. 118, Orig., pp. 757-771.

10. Koetter, K.: Untersuchungen über die Ausscheidung des Salvarsans im Urin bei intravenoeser Injektion konzentrierter wässeriger und konzentrierter Serum-Salvarsan Lösungen, nebst Bemerkungen über den Einfluss der Diurese auf die Salvarsanausscheidung, Med. Klin. **10**:807-809, 1914.

11. Frankel-Heiden and Navassart: Ueber das Schicksal des Salvarsans im Menschlichen Körper, Ztschr. f. exper. Path. u. Therap. **13**:531-542, 1913.

(*c*) Silver arsphenamin, the most recent of the arsphenamin derivatives, is a complex metallic salt produced by interaction between silver salts and arsphenamin, brownish-black in color, readily soluble in water, apparently more toxic to the spirochetes and less toxic to the patient. According to Binz-Bauer-Hallstein, it has the following chemical composition:



It contains the readily oxidizable sodium arsphenamin and the strong oxidizing agent silver oxid in the same molecule.

Arsphenamin and any of its derivatives contains the salt forming radicals NH_2 and OH; the radical $= C_6H_3\text{-}As = As\text{-}C_6H_3 =$ being a chromophor. Arsphenamin may be considered a dye substance. $R_1\text{-}As = As\text{-}R_1$ showing resemblance to the azo radical $R_1\text{-}N = N\text{-}R_1$, N simply substituted by As, can thus be compared to an azo substance and can even possess the yellow color of the simple azo dyes. The primary amin may be diazotized to diazo or tetrazo compounds and be linked with phenols, phenolsulphonate, amins and their derivatives, yielding more complicated substances. Applying reactions of this type, Abelin worked out quite a satisfactory method for the detection of arsphenamin in the urine, maintaining that it is specific for the presence of the $R\text{-}As = As\text{-}R$ radical. It is so simple that it meets the requirements of a clinical method.

The concentrations of solutions required are: (1) hydrochloric acid, 5 per cent.; (2) sodium nitrite solution, 0.5 per cent.; (3) resorcin solution, 10 per cent., and (4) sodium hydroxid solution, 10 per cent.

Technic.—To 5 c.c. of urine, fresh or preserved with chloroform, in test tube 1 cooled in running water or the icebox, are added 0.5 c.c. of the hydrochloric acid solution and 1 c.c. of sodium nitrite solution. The mixture is well shaken and kept cool until the reaction is complete (about ten minutes).

In test tube 2 a fresh mixture of 4 c.c. resorcin solution with 1 c.c. sodium hydroxid solution is prepared. Following Abelin's method the contents of test tube 1 are added to that of test tube 2 and well shaken, producing a distinct red in the presence of arsphenamin in fairly large amounts and a brown clear colored solution in the absence of this substance which soon extends throughout the upper stratum. In our investigation we used the ring

test. In order to carry it out successfully the urine is transferred by means of a 5 c.c. pipet from test tube 1 to test tube 2 which is placed in a slanted position to avoid mixing the two solutions. Two distinct layers are formed with an intervening stratum of pink to red depending on the amount of arsphenamin present; in the absence of arsphenamin no colored ring develops between the two layers. By comparing this colored zone with that produced by solutions of arsphenamin or neo-arsphenamin in known quantities in urine the approximate amount excreted can be determined.

Sensitiveness of the Abelin Test.—With pure reagents and careful manipulation the test is very sensitive, as the results indicate:

	Grams of Neo-Arsphenamin in 10 C.c. of H_2O	Grams of Neo-Arsphenamin in 10 C.c. of Urine
+++	0.001-0.0007	0.001-0.0007
++	0.0006-0.0004	0.0006-0.0005
+	0.0003-0.0002	0.0004-0.0003
⊕	0.0001-0.00009	0.0002-0.0001
○	trace 0.00009-0.00008	0.00009

The color interference due to urinary pigments is slight.

Interference of Other Substances with the Abelin Test.—Leredde and Rubinstein in an unpublished communication suggest the possibility of interference with this test by various other benzene derivatives, such as, for instance: acetylsalicylic acid, acetphenetidin, antipyrin and the salicylates so commonly used. Urine tested by us after internal use of these substances or their direct addition yielded negative results.

Urine from patients suffering with pneumonia, nephritis, rheumatism and gonorrhea was also tested and found to be negative.

CLINICAL STUDY OF THE ABELIN REACTION

Review of the Literature.—In his exhaustive thesis dealing with arsphenamin and its accidents, Jamin [12] states that intravenous injections alone afford a constant elimination which would seem to be the commonly accepted view. We shall therefore limit our discussion to cases in which that method of treatment was used.

Abelin, himself, after studying a number of syphilitic patients in various stages of that disorder stated that arsphenamin and neo-arsphenamin could be demonstrated in the urine by means of his test within from five to fifteen minutes after an intravenous injection. In his cases the test was usually negative within five or six hours thereafter. One patient showed a positive Abelin reaction eight hours after the injection of 0.3 gm. (4½ grains) of arsphenamin, and another patient presented a weakly positive Abelin reaction eleven hours after the injection of 0.4 gm. (6 grains) of the same preparation. Abelin also expressed the opinion that a similar dose when given to one person will cause a marked reaction while in another it will produce only a slight or even a negative response. He examined in all thirty-

12. Jamin: Le salvarsan et ses accidents, Thèse de Paris, 1913.

four cases of syphilis. He does not recommend Ehrlich's diazo reagent as a test for arsphenamin and its derivatives in the urine because it does not give a constant color reaction as does his resorcin test. In his opinion the excretion of arsphenamin and allied substances is undoubtedly related to the patient's general condition. These drugs are eliminated so rapidly that a portion of the dose injected is always passed out unchanged.

In a series of 435 examinations of patients treated with these drugs Leredde and Rubinstein found only eight instances in which there was an abnormal elimination. Their patients were given doses varying from 0.15 (2¼ grains) to 1.2 gm. (18.51 grains) of neo-arsphenamin. In one case of latent syphilis elimination did not begin until twenty-four hours after injection, and it ceased six hours later. In a paretic patient elimination did not appear until two hours after treatment, only to cease quickly and then to reappear at the end of twenty-four hours. Elimination was nil in a case of tabes dorsalis following several Abelin tests; the legs became edematous and treatment was suspended. None of the patients who eliminated abnormally belonged to either the primary or secondary periods. Leredde and Rubinstein found that elimination not frequently began, as evidenced by the reaction under discussion, within five minutes after injection and was completed, as a rule, within twenty-four hours. At the expiration of that period they rarely found a positive Abelin test, especially after a small dose. According to their findings, the elimination is in proportion to the amount injected. On the other hand, its duration depends to a certain extent on the same factor. They further ascertained that in patients who had been given eight, ten and fifteen injections in a course the elimination remained normal.

Escallon recommends the Abelin reaction as a useful means of following in an exact manner the elimination of arsphenamin in the urine. In his opinion, this diazoreaction affords the possibility of assuring one that the amount already given has been passed off, which is of extreme importance if more treatment is deemed advisable. He found that, as a rule, all of the drug was eliminated within forty hours after the initial injection and within fifty-three hours after the second one, while fifty-nine hours was required to eliminate the third dose. Escallon recommends the Abelin test for clinical work in preference to Marsh's and the others more commonly employed because of its simplicity and also because it is sufficiently accurate in most instances. Riebes studied a number of cases of syphilis in which the patients had been treated with arsphenamin and neo-arsphenamin and saw little, if any, difference in their elimination as shown by the Abelin reaction. Following repeated injections, elimination was slower. The tests in thirteen out of sixty-five cases followed in this manner were

positive seven hours after injection. The rest were all negative within seven hours after treatment. In the cases showing slower elimination, nine patients exhibited a positive Abelin test for seven hours while the other four were still positive twelve hours after. Riebes also noted that some cases after being negative would revert to positive, showing that some of the drug was released from time to time and that elimination does not always proceed in a rhythmical manner. He did not find that such factors as the size of the dose, preceding treatment by means of mercury, iodids or arsphenamin, exerted any regular influence on the elimination.

Koetter has employed this reaction in syphilitic patients treated with concentrated neo-arsphenamin injections. Some of them presented a positive Abelin test even six or seven days after injection. He said that almost all of his patients came under one of two classes as regards elimination—those whose urine was negative within six hours, or those who showed a positive reaction for twenty-four hours or even longer. In his experience the elimination in any one case may vary from time to time. His findings were based on results obtained in examining patients after seventy-eight injections. By shaking the tube containing a weak Abelin reaction, Koetter says it will become more apparent. The solvent employed is of importance as regards elimination. Excretion occurred a longer time after serum injections than following those in which the drug was dissolved in water. He quotes Zimmern as saying that dilute solutions of arsphenamin are more quickly eliminated than concentrated ones. Koetter ascertained that 0.3 gm. (4½ grains) of arsphenamin given in water would be eliminated within sixteen hours, while a similar dose dissolved in serum would not be excreted until twenty-seven hours had passed.

Frankel-Heiden and Navassart state briefly that this diazoreaction may still be positive for one or two days after a large dose, as 0.6 gm. (9 grains) of arsphenamin.

Webster does not agree with those who recommend this test. He questions its delicacy and states that arsenic may be found in the urine long after the Abelin test has become negative.

Beisele disputes Abelin's claim that this resorcin reaction is specific for the arsphenamin group in the urine.

PERSONAL CLINICAL STUDY OF THE ABELIN REACTION

We have employed this test in eighty cases of syphilis but shall refer to only fifty of them which have been studied in detail. Practically all of the patients had received neo-arsphenamin in concentrated aqueous solution, the injections being given at weekly intervals. A large majority of the cases were from the private practice of one of us and from the House of Correction. Five were studied at

the Cook County Hospital through the courtesy of Dr. Stillians. Our cases were as follows: primary syphilis 5, secondary 9, tertiary 6, neurosyphilis 5, interstitial keratitis 1, and latent syphilis 26. Taking them up according to this classification, we ascertained that one of the primary cases showed a faint Abelin reaction twenty-four hours after receiving 0.4 gm. (6 grains) of neo-arsphenamin. In another case of this same type the diazoreaction was positive for only six hours after 0.3 gm.

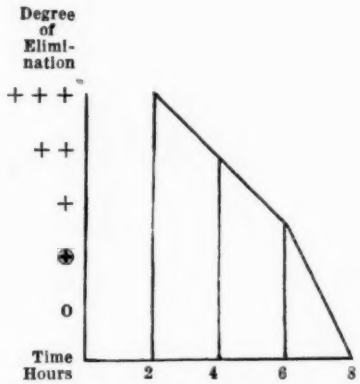


Chart 1.—Primary syphilis. The first injection of 0.3 gm. (4½ grains) of neo-arsphenamin was followed by sore throat and a fever (104.5 F.). These soon subsided.

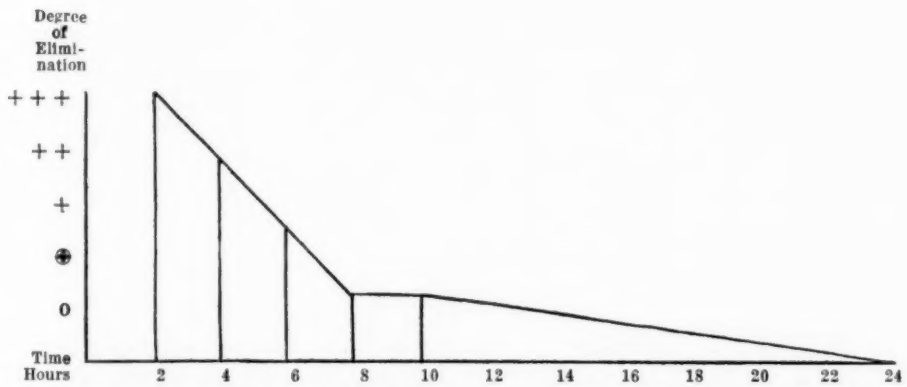


Chart 2.—Primary syphilis. Degree and time of elimination after the fourth injection of neo-arsphenamin, 0.6 gm. (9 grains).

(4½ grains) of neo-arsphenamin (Chart 1), while the third patient with a case of primary syphilis showed a faintly positive Abelin test for ten hours after an injection of 0.4 gm. (6 grains) of neo-arsphenamin (Chart 2).

Of the secondary cases, in all but two there were positive reactions twenty-four hours after the injections. One patient exhibited a negative

Abelin test within four hours after receiving 0.3 gm. (4½ grains) of the sodium diarsenol brand of arsphenamin. Another patient exhibited a weakly positive Abelin test after twenty-four hours, while still another patient was negative at that time (Charts 3, 4 and 5). Four other cases belonging to the secondary group showed merely a trace at the end of twenty-four hours.

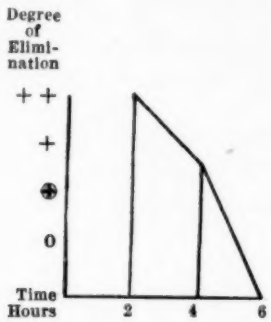


Chart 3.—Secondary syphilis. The first injection of neo-arsphenamin, 0.3 gm. (4½ grains), was followed by headache and a feeling of weakness.

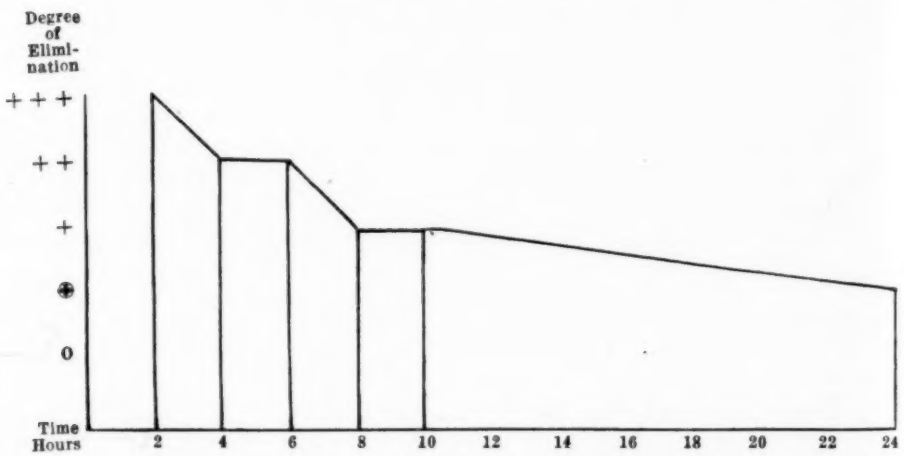


Chart 4.—Secondary syphilis. Degree and time of elimination after the second injection of neo-arsphenamin, 0.6 gm. (9 grains).

The tertiary cases were of interest in that all of them were positive twenty-four hours after injection. One tertiary patient's urine presented a 1+ Abelin reaction twenty-four hours after injection, two others were 2+ at the expiration of a like period while a fourth case was still 2+ thirty-six hours after receiving 0.45 gm. (6¾ grains) of neo-arsphenamin (Chart 6). The others just referred to had received 0.45 gm. (6¾ grains), 0.6 gm. (9 grains) and 0.9 gm. (13½ grains), respectively.

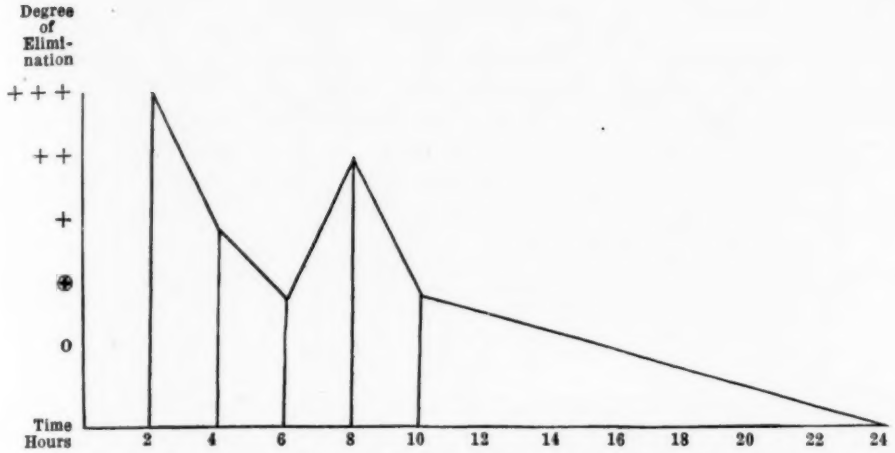


Chart 5.—Secondary syphilis. Degree and time of elimination after the first injection of neo-arsphenamin, 0.45 gm. (6¾ grains).

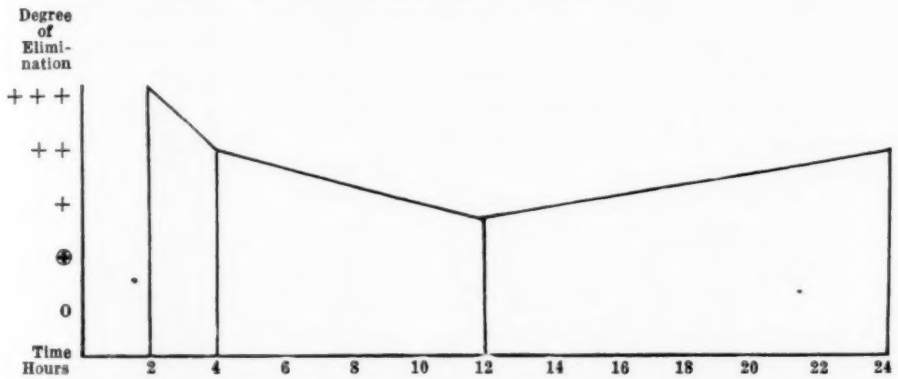


Chart 6.—Tertiary syphilis. Degree and time of elimination after the second injection of neo-arsphenamin, 0.45 gm. (6¾ grains).

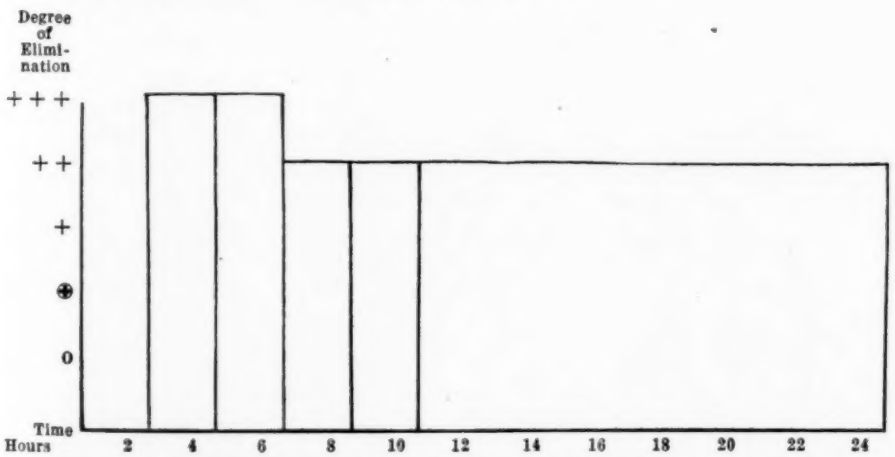


Chart 7.—Tabes dorsalis. Marked increase in fulgurating pains for forty-eight hours after the first injection of neo-arsphenamin, 0.15 gm. (2¼ grains).

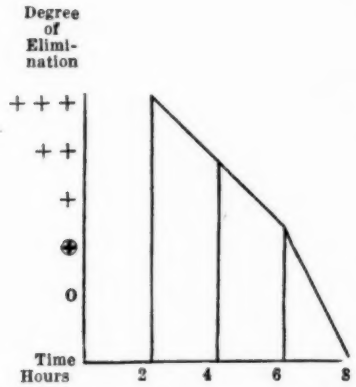


Chart 8.—Incipient paresis. Degree and time of elimination after the fifth injection of neo-arsphenamin, 0.9 gm. (13½ grains).

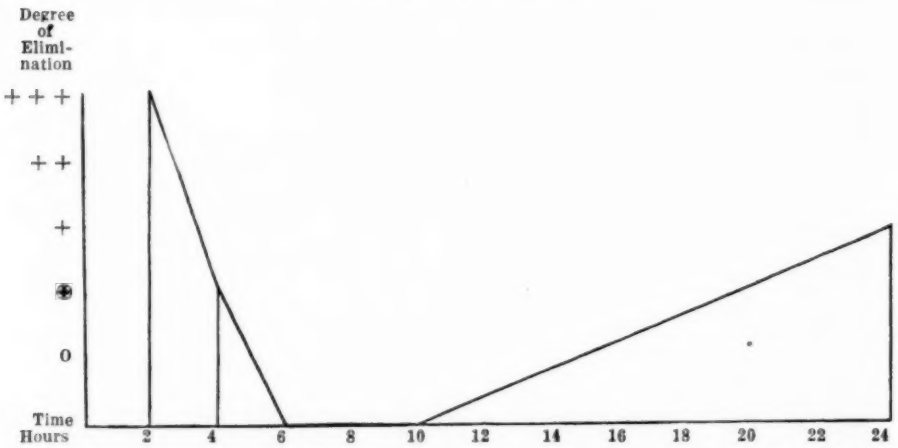


Chart 9.—Latent syphilis. Degree and time of elimination after the third injection of neo-arsphenamin, 0.9 gm. (13½ grains).

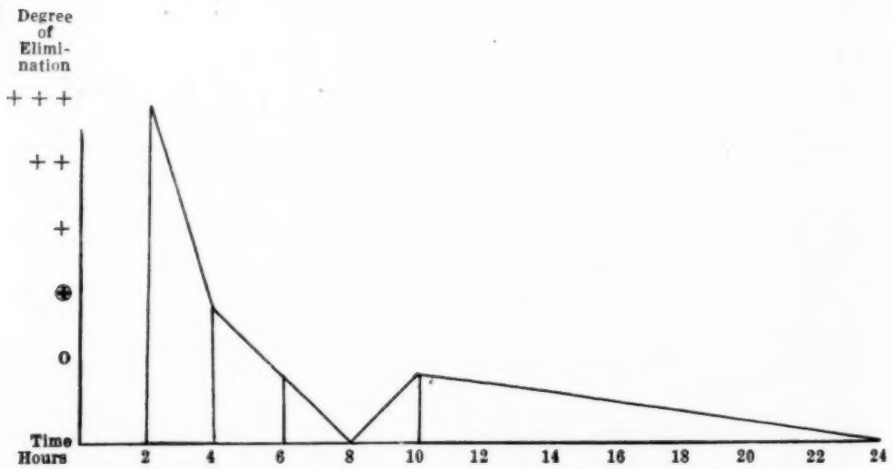


Chart 10.—Latent syphilis. Degree and time of elimination after the second injection of neo-arsphenamin, 0.6 gm. (9 grains).

Two of the five cases of neurosyphilis gave interesting responses to the Abelin test. One patient with cerebrospinal syphilis showed a 2 + reaction twenty-four hours after receiving 0.9 gm. (13½ grains) of neo-arsphenamin, while a patient with an advanced example of tabes dorsalis gave a similar response at the expiration of an equal length of time, but after a small dose, 0.15 gm. (2¼ grains) of neo-arsphenamin (Chart 7). A patient with early paresis (Chart 8) showed only a trace six hours after an injection of 0.9 gm. (13½ grains) of neo-arsphenamin. Fifteen of our latent syphilitic cases were positive twenty-four hours after the injections (Charts 9 and 10). One latent case was 1 + twenty-six hours after a 0.9 gm. (13½ grains) dose. Immediately after this injection the patient partook of a hearty meal and soon afterward became quite ill, suffering from nausea, vomiting and diarrhea which passed away the day after. He had previously received four injections without any untoward symptoms or prolonged elimination so his indiscretion in eating was doubtless an important factor. Our patient with tabes whose Abelin reaction was so pronounced after 0.15 gm. (2¼ grains) dose of neo-arsphenamin suffered no inconvenience after his injection except an accentuation of the fulgurating pains for twenty-four hours, which would seem to indicate a Herxheimer reaction as a result of the antisyphilitic treatment.

As a rule, the initial dose was quickly eliminated, although two patients already mentioned, one with tertiary syphilis and one with tabes, showed a strong diazoreaction for some time (in the first instance thirty-six hours and in the other one twenty-four hours after their first injections). A negress presenting annular papular syphilids showed a negative Abelin reaction within four hours after receiving 0.3 gm. (4½ grains) of the sodium diarsenol brand of arsphenamin. A negro with similar skin lesions gave a negative response to the resorcin test at the end of twenty-four hours after a 0.6 gm. (9 grains) dose of neo-arsphenamin. A patient with a well-marked case of tertiary syphilis showed a strongly positive Abelin reaction for twenty-four hours after a first injection.

Approximately one-half of the patients examined after their second injection showed a trace of arsenic after twenty-four hours. Most of our patients with latent cases had received a number of intravenous injections of arsphenamin or neo-arsphenamin. About 60 per cent. showed a positive Abelin reaction at the end of twenty-four hours after treatment. One of these patients had received, just previous to our examination, a weekly injection of 0.9 gm. (13½ grains) of neo-arsphenamin or a total of 7.2 gm. (138.87 grains) during a period of eight weeks. There was only a trace of color in the urine when the resorcin test was applied. Several patients who had received similar therapy did not show any material difference in respect to the Abelin reaction.

Greven had stated that when mercurial preparations are administered previous to arsphenamin the elimination of the latter is retarded. Thus, in his experiments, healthy guinea-pigs which had received no mercury would eliminate arsenic for from fifteen to eighteen days while those animals to which mercury had been previously given would excrete arsenic for from twenty to twenty-five days. Since all of our patients except two had been given mercury beforehand, we can say little in this connection. One of the two was negative to the diazoreaction after four hours, while the other still showed a trace of arsenic after twenty-four hours.

CONCLUSIONS

1. The Abelin test seems to be of real value. This opinion is quite generally shared by those who have employed it. In a recent personal communication Leredde again subscribes to this view.

2. The slightly modified Abelin test, as employed by us, is readily and successfully applied for quantitative results without much difficulty or expense.

3. The sensitiveness of the test is very great.

4. It is only positive in the presence of arsphenamin and its derivatives, the quantity being approximately indicated by the color of the ring.

5. Other chemical substances of the benzene series which may be eliminated did not furnish any positive reactions.

6. Urine from cases of pneumonia, nephritis, rheumatism and gonorrhea did not furnish any positive reactions with this resorcin reaction.

7. The elimination of arsphenamin and its derivatives by way of the urinary tract was slower in most of our cases than in Abelin's series. It was usually complete or nearly so within twenty-four hours after injection. A number of cases tested at later intervals gave, with the exception of those mentioned, uniformly negative findings.

8. Elimination was especially prolonged in our cases of tertiary syphilis and neurosyphilis.

9. The apparently early elimination of these drugs would seem, in certain cases at least, to warrant a shorter interval between injections, as has been suggested by Pollitzer, Sicard and others.

10. In cases of apparent nonelimination of the drug evidenced by a persistently negative Abelin reaction one should, as Leredde suggests, make a careful examination of the patient before continuing with the treatment.

11. Elimination seems to be subject to the influence of a number of factors, among them: (*a*) the dose injected, (*b*) the solvent employed, (*c*) previous treatment especially by arsphenamin or its derivatives, (*d*) dietary indiscretion soon after treatment, (*e*) the personal element.

12. Elimination does not always proceed in a rhythmical manner.

7 West Madison Street.

ITCHING IN SYPHILIS*

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Sabouraud has jestingly maintained that a series of two hundred dermatologic aphorisms would amply cover all known practical facts in the field. He included in his list the statement, "Itching lesions are nonsyphilitic," and he qualified this by the modification that of course some syphilitic lesions itched, but that in general they did not.

A search of the literature relevant to the theme of this paper was virtually fruitless. Except for the conventionally known facts that the small papular secondary syphiloderm, or syphilitic lichen and its derivatives, such as syphilitic acne, may itch, and particularly so in the negro, and that syphilids in general are slightly more likely to be pruriginous in blacks than in whites, I found only one reference (and this a most fragmentary one) to the subject in general. Phineas Abraham [1] in discussing pruritus in syphilis states, "This is particularly apt to occur on the scalp, scrotum and perineum, and the front of the legs, as well as when the syphilid happens to be complicated with eczema or other pruritic skin affection. Very rarely, a pure syphilid may be intensely pruritic." The same author, in the same work,[2] says of leukoplakia of the prepuce, that the resulting shrinking "is often accompanied by severe soreness and itching." In an effort to gather further data, I communicated with several syphilologists throughout the country, requesting pertinent references or reports of personal experiences. Only Dr. Herrman Goldenberg was able to recall a case, in the late Dr. Fred Leviseur's clinic at the Mount Sinai Dispensary, in which intense pruritus had accompanied multiple gummas of the forearm. Since pruritus is regarded as a symptom almost excluding the diagnosis of syphilis, I should like to report a case which illustrates the diagnostic danger of too unqualifiedly accepting this belief.

REPORT OF CASES

History.—I. M., married, a merchant, aged 49, consulted me on Aug. 12, 1920, for an itching scrotal eruption of a year's duration. The lesions gradually increased in number on the scrotum, and were also present sparsely elsewhere, one on the right wrist, one on the lower right abdominal quadrant. For

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* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

1. Abraham, Phineas, in Power and Murphy's System **5**:10.
2. Idem. **5**:153.

a year the terminal phalanges of the right index finger had been red and swollen and painful, and the distal articulation was almost immobile.

The scrotal lesions itched intensely and almost continuously, both day and night. At times the finger pained. The man had had gonorrhea thirty years before, but denied syphilis, and a Wassermann test performed two months after the onset, or ten months prior to his first visit to me, had been negative. Aside from this, his clinical history contained nothing bearing on his skin lesions.

Scrotal eruption.

Examination.—The scrotum was studded with flat, annular violaceous or purple lesions, varying in diameter from 1 to 2 cm. They were infiltrated, elastic and had a sharp margin, the rims of which were higher than the depressed or cup-shaped centers. Even where lesions were not visible, they could be felt as small disks inserted in the cutis. A single, annular lesion existed on the right lower abdominal quadrant, and a scar on the right wrist, which the patient said was the result of a lesion like those on the scrotum, that had become a boil. The right index finger was twice its normal circumference, red and above the second joint infiltrated. The last joint was tender and practically fixed.

Diagnosis.—Granuloma annulare, despite the unusual location, with possible tuberculosis of the finger, or hypertrophic annular lichen planus was considered. A microscopic study excluded lichen planus, and supported the concept of granuloma annulare, or sarcoid of Darier-Roussy.

Comment.—The general physical examination was negative. No thoracic signs of tuberculosis were found. The abdominal viscera seemed normal. The lymph glands were impalpable, the oculomotor system was functioning properly, and the deep tendon reflexes were slightly exaggerated. A roentgenogram of the diseased finger showed that the bones and the periosteum were unaffected.

Treatment and Course.—It was decided to base treatment on the presumptive diagnosis of granuloma annulare. Roentgen irradiation was begun with a Holzknecht unit, August 20 and until September 18 this was continued at weekly intervals, five exposures having been made. At the same time, arsenous oxid pills, beginning with 1/50 grain three times daily, in increasing doses, were prescribed. Various local antipruritics were used. By September 27, no impression had been made on the lesions, and the suspicion of syphilis was reawakened. Infection was again denied, and the serum test proved faintly positive (+) with cholesterinated antigen, and negative with alcoholic antigen. Nevertheless, the therapeutic diagnostic test was decided on, and a grain of mercury salicylate was injected October 1. Three days later the patient stated that several hours after the injection the finger had become redder and more painful and that itching in the scrotum had stopped the same night. October 4, arsphenamin (0.4) was administered. By October 8, or after one mercury and one arsphenamin injection, the swelling in the finger was reduced by half, and the pain had vanished. October 11, the scrotal lesions were one third their original size, and by October 15, they were gone. Routine combined arsenical and mercurial treatment in series was instituted, but after a rest period beginning December 13, and ending January 10, 1921, the Wassermann reaction was +++. Since then the patient has had two series of mercuric oxycyanid injections of 1/12 grain, intravenously, twenty-seven treatments in all. Between the two series, the Wassermann reaction was found to be ++++.

COMMENT

The outstanding features of this report are the negative history, the negative serum test, the atypical character of the lesions, and above all their itching. Every fact negated the likelihood of syphilis, including the minute anatomy of the lesions, and only the therapeutic diagnostic procedure, with provocation of the Wassermann test, finally solved the problem. Without precisely seeing how the error in diagnosis could have been avoided, considering the misleading data, I cannot entirely relinquish the thought that it was the belief that itching almost precluded syphilis that most surely dulled clinical astuteness.

Phineas Abraham mentions, as already noted, that scrotal lesions may itch. The case herein reported supports the British writer's statement. Furthermore, it was a pure syphilid, one uncomplicated by any other itching dermatosis. Early syphilis is often seen in con-

junction with scabies, and undoubtedly coexists with many other itching eruptions. In such an event, it is rarely difficult to make a correct clinical distinction between the two elements in the picture. But it is important to realize that certain syphilids themselves itch, and so not to be thrown off the track as I was when confronted with the phenomenon. Neither the appearance, nor the roentgenogram of the finger suggested syphilis. The infiltration must have been hypodermal.

OTHER CASES

At the Mount Sinai Hospital, Dr. Goldenberg and I were requested to see a woman with fingers exactly like this man's. Radiographs showed normal phalanges, but her Wassermann test was positive. The lesions disappeared under specific treatment. Instances of this sort show the futility of judging syphilis by classic standards.

Unfortunately, the most instructive cases often elude us, or I should be able to give a complete report of another baffling pruriginous syphilid. The patient was a middle-aged Austrian in the skin ward of the old German Hospital in New York. He had a generalized, intensely itching dermatosis of many years' duration, which resembled exfoliative dermatitis on a seborrheal basis. A biopsy was made, for it was thought that microscopic study might reveal the true nature of the condition. An astonishing degree of inflammation and thickening were found in the arterioles, and a lymphocytic perivascular infiltration with a few plasma cells. This so much more suggested syphilis than any of the erythrodermas, or the ordinary chronic scaling or vesicular diseases, that the patient was questioned as to syphilis, and admitted a presumptive infection in his youth. His Wassermann test was doubtful (+ —), but he was given an injection of mercury salicylate, and that night his itching stopped for the first time in years. Within a week, having received a second injection, his eruption had nearly completely disappeared, although all local treatment over a number of years had failed to relieve him. He then promised to visit me for further study, but failed to.

This patient's eruption resembled syphilis even less than does granuloma annulare. It itched as intensely as did the eruption in the first case, but, as in the first case, the Wassermann test was doubtful. Whether it would have been provoked by further treatment cannot be stated. If Bruusgaard's case of cutaneous tuberculosis resmbled pityriasis rubra (Hebra), it is not astonishing that, however rarely, syphilis may also resemble exfoliative dermatitis, and undoubtedly the same holds true of syphilitic mimicry of the ringed eruption. The amazing feature in both of the patients was intense pruritus which yielded promptly to trivial antispecific treatment. The

itching stopped in each instance a few hours after the first injection of mercury, the involution of the lesions themselves rapidly following the usual course.

780 Madison Avenue.

ABSTRACT OF DISCUSSION

Dr. William Allen Pusey, Chicago: I recall in my experience a practically duplicate case of Dr. Highman's scrotal case of itching syphilis. The patient was a middle aged man who came to me with the diagnosis of eczema. He had an infiltrated surface, with annular lesions, the whole condition having existed for a long time. It cleared up almost miraculously under specific treatment. I think it is hardly to be called an itching syphiloderm. While it is the syphiloderm that itches, the itching is probably due to the friction and the warmth which produced irritation. It does not seem to me to come in the same category as the itching, small, folliculopapular syphilid.

Dr. Henry H. Whitehouse, New York: A case strikingly like Dr. Highman's was under my observation some twenty-three years ago, but I have never seen a second, so concluded that such cases are rare.

My case differed from Dr. Highman's in being a frank, straightforward secondary syphilid, generalized sparsely on the body and markedly on the arms. It had the brownish ham color, the distribution and grouping, so that clinically there was no mistaking its character. It was before the days of the Wassermann test and the striking symptom the woman complained of was intense itching which was so pronounced that she was fairly maniacal. She had no accompanying itching dermatitis. Under antisyphilitic treatment the itching ceased rather promptly as the eruption subsided and disappeared. Of course the itching of the early roseola is a common observation.

Dr. August Ravogli, Cincinnati: In the past we were taught that itching was never present in syphilitic eruptions, that this was one of the signs of differential diagnosis, with the exception of the mucous patches or condyloma planum which was accompanied by a distressing itching sensation. We often see the condyloma in the breast and crurogenital region, always accompanied by the itching, on account of the abrasions and the irritation caused by perspiration and seropurulent secretion.

I agree with Dr. Pusey that sometimes in the beginning of the small papular syphilid there is an itching sensation that the patients complain of, and it would suggest an association with lichen, if it were not for the other symptoms.

Dr. James Herbert Mitchell, Chicago: In a series of papers in the last two years Leredde has called attention to the occurrence of itching in syphilids and also the rôle played by syphilis in eruptions, in even neurodermatitis. He is convinced that in some cases they are of syphilitic origin. He began by a theoretic discussion, and in the last paper gave case histories that show that ordinary itching dermatoses are of syphilitic origin.

Dr. Walter J. Highman, New York: I think Dr. Pusey's criticism is well founded and his remarks are based on a group of cases that Phineas Abraham refers to as complicated by other dermatoses, but I believe in my case the criticism does not hold true, for the following reasons: In the first place, all the antipruritics used had no effect on the pruritus. That, I think, eliminates the hypothesis that any secondary dermatosis caused the itching.

In the second place, the fact that the itching disappeared within a few hours after beginning antisyphilitic treatment supports the belief in its specific origin. For this reason, together with the fact that there was no itching eruption associated with the lesions, I concluded that this was a unique case, in that it was a pure syphilid with itching. There was nothing in the histologic section to show what caused the itching, but neither is there in many other disorders.

ORIENTAL SORE

REPORT OF FOUR CASES

D. KING SMITH, M.D.
TORONTO, CANADA

Oriental sore is endemic in Asia, Africa, South America and southern Europe. The lesion is caused by *Leishmania tropica.* Infection is conveyed to the human subject through abrasions or small wounds, probably by insects. Autoinoculation is common. Early stages show nodules, which break down to form ulcerating and vegetative lesions.

Clinically, one finds that after an incubation period lasting from a few days to several weeks, one or more itching spots appear on uncovered parts of the skin. These lesions become indurated, and may develop to the size of a bean. The nodule then breaks down, forming an ulcer which becomes crusted. The edges of the ulcer are sharp, the base irregular and covered with yellowish-red granulations. After an indolent course, the ulcer heals by scar formation.

The following cases came under my observation last summer:

REPORT OF CASES

CASE 1.—*History.*—D. E., aged 4 years and 2 months, had a hard papule about the center of each cheek, which the mother noticed while in Bagdad, about February 10. Six weeks later, one appeared also on the tip of the left ear. The papules soon broke down, developing into running sores.

Examination.—June 28, the lesions presented the following characteristics: Those on the face were annular and about half an inch in diameter, with a well marked inflammatory areola. The crust was of a dark color and very adherent. On removal, there was no pus, but a dark red granular base, showing considerable ulceration. The lesion on the ear showed much destruction of tissue, a large part of the area being covered with a crust similar to those on the face. There was no glandular enlargement. Except when the lesions were rubbed or struck, there was no pain.

Treatment.—During the first two weeks, while under my care, boric acid compresses were applied during the day and ammoniated mercury, 10 grains to the ounce of petrolatum at night. There was no evidence of improvement under these applications. A 5 per cent. argyrol solution was used over a period of two weeks, with no improvement. The patient had three roentgen-ray treatments and one injection of 0.25 gm. of novarsenobenzol (Billon), a brand of neo-arsphenamin. One week after the injection, the crusts on the left cheek and ear became detached, leaving healthy looking ulcers. A week later, the crust on the right cheek also became detached. Four weeks from the time of the injection, all of the sores had healed, with marked scar formation.

Fig. 1.—Lesions of patient in Case 1.

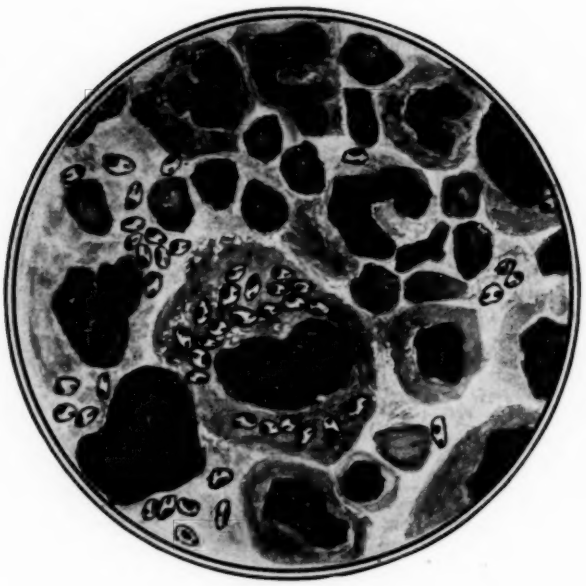

Fig. 2.—Leishman-Donovan bodies in large lympho yte.

CASE 2.—Miss W., a nurse, while on board ship, a short time after leaving Bagdad, noticed a small sore on the upper part of the right cheek. A month later a similar one appeared on the right wrist. The progress of the sores and the characteristics were similar to those described in the previous case.

Treatment could not be carried out in this case as the patient was out of the city during the summer.

CASE 3.—E. E., a girl, aged 7 years and 10 months, left Bagdad the last of March with the two other patients. There was no evidence of any skin lesion until after she arrived in Canada; that is, about ten weeks after leaving Bagdad. The lesion when first seen had the appearance of an ordinary impetigo, situated just below the left ear. However, the crust was firmly attached and removed with difficulty, leaving a blood-clot-like surface.

The patient was under my observation for a month. During this time, the extension of the ulcer was very slow.

Treatment could not be carried out in this case.

CASE 4.—Mr. E., aged 40, father of the children (Cases 1 and 3) left Bagdad the middle of May. After he had been in Canada two weeks, there appeared on the left wrist a hard "pimple," which remained as such for about two months. It then broke down and spread rapidly. At the end of four weeks, it was about the size of a fifty-cent piece, presenting a marked inflammatory areola.

He soon had to return to Bagdad, so treatment was not carried out.

Bacteriologic Findings (By Dr. Hamnett A. Dixon).—Films were obtained by removing the crusts and applying glass slides to the oozing surfaces. Giemsa's and Wright's staining methods were used.

The parasites were found in the endothelial cells and also lying free. They occurred as round, oval or pyriform bodies, measuring from 2 to 4 microns by 1.5 to 2 microns. The protoplasm appeared to be finely granular and to contain two nuclear structures, one large and round, the trophonucleus, usually situated toward the center; the other small and bacillary in shape, the kinetonucleus, situated near the periphery of the cytoplasm.

CONCLUSIONS

1. From this series of cases, the inoculation period varies from six weeks to two months.

2. The condition is autoinoculable.

3. Roentgen-ray treatment with arsphenamin or neo-arsphenamin is worthy of a trial.

4. Castellani believes that cutaneous leishmaniasis even in mild form is not merely a localized condition, but that there is a general infection. In the cases described there was no evidence of any general infection.

ABSTRACT OF DISCUSSION

DR. ERNEST L. MCEWEN, Chicago: In the case which I reported at our meeting some years back, the use of arsphenamin had practically no result. The patient was given, I think, three doses.

I would like to ask Dr. King Smith whether in the smears there were found any of the intracellular diplococcus-like bodies which were present in the case I reported, and which have been reported in a number of cases by other observers.

Dr. Louis B. Mount, Albany: I had occasion to see perhaps one of the most unusual types of skin infection with the Leishman-Donovan bodies. The patient, an Italian, had had a fall, followed by the development on the forehead of a most peculiar looking lesion. The lesion was about 1 inch long, and half an inch wide. There was no crust formation. It was slightly elevated, with a sort of warty, pinkish surface. It looked so much like an area of tuberculosis that a biopsy was made and the material was sent to Dr. Ewing for examination. He stated that he was about to report that it was an endothelioma, because of the endothelial proliferation, when his eye was caught by a peculiar granulation in the endothelium. Staining with protozoal stains brought out clearly the presence of these Leishman-Donovan bodies.

Dr. Walter J. Highman, New York: Recently in New York, Dr. Fox had a case like that reported by Dr. King Smith, in a boy just returned from service. We were able to demonstrate the Leishman-Donovan bodies quite as well as in Dr. King Smith's case. A similar case was shown before one of the societies. I rather think our eyes are getting keener, or else the cases are more plentiful since the war.

Dr. Jay Frank Schamberg, Philadelphia: Quite a series of cases of inguinal granuloma have been seen recently in Philadelphia and have been regarded as leishmaniasis.

Dr. Fred Wise, New York: I would like to ask Dr. King Smith one question: Did one of these patients get it from the other on shipboard, or did they get it individually while residing in Arabia? Is the disease easily contagious?

Dr. David King Smith, Toronto, Canada: In reply to Dr. Wise, my impression was that the cases all started in Bagdad.

As to Dr. McEwen's question: I did not see the intracellular diplococcus.

EPITHELIOMAS OF THE FACE AND THEIR TREATMENT WITH RADIUM *

HOWARD MORROW, M.D.
AND
LAURENCE TAUSSIG, M.D.
SAN FRANCISCO

Chronic lesions of the face are of great importance to dermatologists on account of their frequency and because the patient expects not only a cure, but a good cosmetic result. In patients past the fourth decade, epitheliomas make up a large percentage of these chronic lesions. The two great classes of skin cancer occurring on the face are the basal-cell epitheliomas and the squamous-cell epitheliomas. The first is by far the most common. It fortunately can usually be diagnosed at a glance and is the most readily cured. The squamous-cell type often presents more difficulty in diagnosis and the prognosis should always be guarded, because it is this type in which there is a tendency to lymphatic involvement.

CLINICAL FACTS REGARDING EPITHELIOMAS

It is not our purpose to enter into a discussion of the etiology of epithelioma, but a few clinical facts may not be amiss. In the first place, it is striking that the great majority of these lesions of the face are associated with numerous keratoses and a seborrheic skin. It is, of course, not possible to state with certainty when seborrheic keratoses become cancerous; for they may be present for years before showing evidence of malignancy and, again, a single keratosis may change to an epithelioma in a few weeks. It is quite evident that keratoses develop most frequently in those exposed to the elements, as farmers and sailors. The rather uncalled for names of "sailor's cancer" and "farmer's cancer," applied to cases of epithelioma developing in men following these occupations, are merely specific instances of the malignant degeneration of keratoses due, in part, to exposure. The influence of chronic irritation in the production of epithelioma, particularly of the lips, is not proved by statistics of large numbers of cases to be more than a predisposing factor. Once a malignancy has developed, it is certain that chronic irritation increases the rate of growth. This is seen particularly in the cases of rodent ulcers which become much more active under inefficient treatment with cautery, freezing, electrolysis, roentgen ray, radium or surgery. The development of epithelioma on the basis of

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

Fig. 1.—Leukoplakia of lip or early epithelioma; very superficial thickening; 10 mg. full strength plaque, aluminum 0.1 mm., total two and one-half hours.

Fig. 2.—Epithelioma of lip; infiltration limited to mucous membrane; 5 mg. half strength plaque, rubber only, total two hours; three bare tubes, total 2 mc. into the mass.

chronic lesions, especially lupus vulgaris and roentgen-ray atrophy, is well known and of frequent occurrence. It is interesting to note that basal-cell epitheliomas of the face are much more common in men than in women, but with the exception of epithelioma of the lip, this does not appear to be true for the squamous-cell epitheliomas.

The most common type of epithelioma of the face, as stated before, is the basal-cell type or rodent ulcer. The typical clinical features are: a history of long duration, usually of years; a rolled waxy border with fine telangiectases, with or without ulceration, and the absence of metastases. The malignancy consists in a tendency to extend to and destroy neighboring structures, a liability to recurrence when insufficiently treated and the frequency with which the ulcer occurs in inaccessible positions. Basal-cell epitheliomas should be subdivided clinically into the rodent nodule, the superficial ulceration, the deep ulceration and the cicatrizing variety.

VARIOUS METHODS OF TREATMENT

The types of basal-cell epithelioma which present special difficulty are the very extensive ones, with or without bone involvement, and those involving the canthi or the lids of the eyes. The very extensive cases are the result of neglect on the part of the patient, or, even more frequently, are due to inadequate treatment by incomplete removal or superficial cauterization. Inefficient cauterization is usually represented by the use of a relatively superficial chemical caustic. Deforming rodent ulcers in which large portions of the face have been destroyed are becoming much less common. This is probably due to the greater knowledge of the general practitioner and to the education of the laity to look with suspicion on any enlarging nodule or chronic ulceration. The successful eradication of any extensive epithelioma, especially when the underlying bone is involved, will necessarily involve the production of a considerable amount of deformity. Rodent ulcers involving the canthi, even when small, are to be handled with care because of the danger of injuring the eye and the probability of extension into the orbit if the growth is not entirely destroyed. Epitheliomas of the eyelid are usually of the rodent nodule type, relatively deeply situated. They must be treated by some means which will obviate the destruction of the lid, because plastic surgery at best cannot give a good result if there has been much loss of tissue.

The great majority of dermatologists are now ready to admit that in most cases of basal-cell epithelioma, radiotherapy alone or in combination with curettage is the treatment of choice. The advantages of radium in the average case are that it is painless in application, the resulting scar is the smallest possible and recurrences are as few following proper radium therapy as following any other form of treatment. The one disadvantage in these cases is the time that it takes. It is in

Fig. 3.—Same patient as Fig. 2; ten days after starting treatment, showing reaction.

Fig. 4.—Diffuse superficial epithelioma involving entire vermilion border of lower lip; 115.4 mc. in four tubes, silver 0.5 mm., one hour to surface; four bare tubes, total 3.2 mc., buried.

the extensive and difficult cases which have been mentioned that radium stands out as the only satisfactory form of treatment. When bone is involved the use of radium can frequently bring the process to a standstill even when it is impossible to produce a cure. In these cases it is probably best to curet out as much of the involved bone as possible, following which radium in the form either of plaques or tubes should be applied for a sufficient time to produce a shallow bone necrosis. This often leads to the formation of a sequestrum, and after removal healing may take place, following which plastic surgery may be employed. In very extensive cases the application of radium can usually accomplish a rapid clinical cure, which, however, is followed frequently by small recurrences for which we must be constantly on the lookout. It is often impossible to irradiate lesions on the lids without giving the sclera a considerable dosage, but this need not deter us, because the resulting reaction clears up readily.

TREATMENT OF RODENT ULCERS

In treating rodent ulcers of the face, surface applications of plaques or tubes of either radium salt or of the emanation are to be preferred to burying needles or bare tubes of emanation. The use of needles or bare buried tubes is rarely indicated because they cause a large amount of scarring and are no more efficient in these superficial lesions than the surface application. The only exception to be noted is in the case of the deep rodent nodule which is refractory to the usual form of radium treatment. This is occasionally found at the canthi where infiltration may be deep, as the result of time or inadequate treatment. In treating a superficial rodent, a full strength plaque, screened with rubber dam only or with 0.1 mm. of aluminum, is fastened over the lesion for a total dose of from three to four hours, divided between two or three successive days. This dose may be given at one sitting, but this increases the reaction without improving the result. If the lesion is relatively deep, from 0.3 to 0.5 mm. of brass is employed as a screen and the time increased to five or six hours. If tubes are used the dosage is roughly 40 millicurie hours per square centimeter of surface, the tubes being distributed as nearly as possible so that there is one tube to each square centimeter. The usual screen when tubes are utilized is 0.5 mm. of silver and 1 mm. of rubber tubing. Any of these methods produces a severe reaction, starting on from the seventh to the tenth day and reaching the height at the end of the second week. Exudation and crusting occur and finally, about the sixth week, the last crust comes away leaving a smooth, white, supple scar. It is, of course, necessary to irradiate the edges of the rodent thoroughly and any attempt to screen the surrounding tissues to lessen the area of reaction leads to a poor result. In

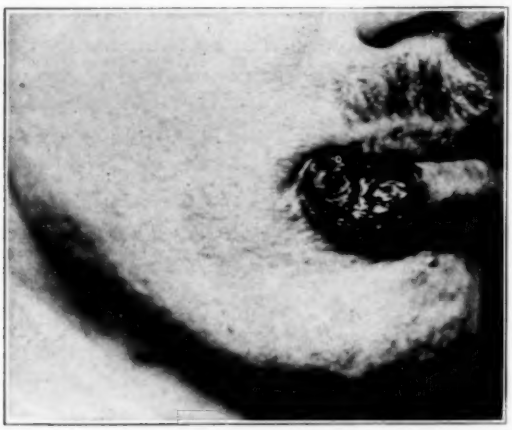

Fig. 5.—Deeply infiltrated epithelioma; hard, discrete glands, palpable; surgical removal.

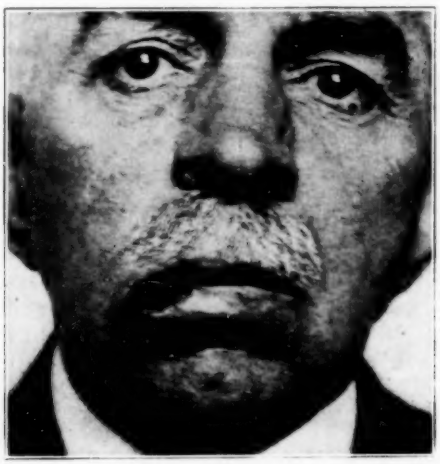

Fig. 6.—Deeply infiltrated epithelioma; no palpable glands; operation refused; five bare tubes, total 8.7 mc., inserted into mass; 10 mg. full strength plaque, brass 0.3 mm., two and one-half hours.

the few cases in which it is necessary to use bare buried tubes, the dosage should be conservative, that is, one or two tubes of 0.5 millicuries each or less may be inserted into the mass, and this is augmented by screened applications to the surface. The great advantage of radium over roentgen ray is that the most severe reaction with the first eventually clears up without undue scarring, while any reaction beyond a faint erythema from the latter may lead to disastrous after-effects, the least of which are telangiectases and the worst of which is a new and more malignant carcinoma.

EPITHELIOMAS OF THE EAR AND OF THE LIP

Epitheliomas of the external ear are of special interest because they present considerable difficulty both in treatment and in diagnosis. The differential diagnosis between squamous and basal carcinoma of the ear is at times impossible without a biopsy. It is clinically true that squamous epitheliomas of the ear are usually less malignant than those occurring elsewhere, in that their growth is slow and involvement of the neighboring lymph glands is late. Satisfactory surgical treatment of malignant lesions of the ear involves a considerable loss of tissue and a poor cosmetic result. It has been reported that radium treatment of lesions of the ear is unsatisfactory on account of the intractable reaction following adequate treatment. It has been our experience that the reaction following radium therapy of cancer of the ear is rather severe and more painful than elsewhere; but this usually clears within a reasonable time. The results, particularly in the smaller and superficial cases, have been good. The technic in the treatment of epitheliomas of the ear is similar to that of superficial epitheliomas elsewhere, except that thicker screens should be used and the time increased correspondingly. Buried bare tubes should only be used in very extensive fungating cases. Unless one is sure that he is dealing with a basal-cell type, the regional lymph nodes should be irradiated with the roentgen ray in spite of the fact that the squamous-cell type in this locality metastasizes late.

Until recently the treatment of carcinoma of the lip has always been surgical. At the present time, surgical treatment is usually efficient in curing those cases in which the growth is limited to the lip, but the operative technic must be perfect, particularly in reference to the excision of a suitable margin of normal tissue with the neoplasm.

Many epitheliomas of the lip commence as keratoses, and it is frequently impossible to differentiate a keratosis from an early malignancy. The differential diagnosis in difficult cases can often be made by palpation. A deep, tight keratosis is never cleared permanently by the application of ointments, and even superficial cauterization may prove insufficient. Such a lesion clears promptly and permanently under adequate radium therapy, and surgery is unneces-

Fig. 7.—Squamous-cell epithelioma of nose tip and septum involving part of upper lip; three bare tubes, total 3.3 mc., buried into lip; plaques to surface, aluminum 0.1 mm., total ten hours.

Fig. 8.—Same patient as Fig. 7, one month after starting treatment.

Fig. 9.—Malignant papilloma of neck; sixteen bare tubes, total 15 mc., buried in mass: Rodent ulcer of cheek; 10 mg., 2 mm. lead, 1 cm. distant, for fifteen hours. Both lesions developed on the basis of a scar following a burn.

sary. A half or full strength plaque of sufficient size to cover the keratosis, screened with 0.1 mm. of aluminum, applied for a total of two to three hours, has proved satisfactory.

The early epithelioma of the lip, in which the mass is distinctly palpable, but which is apparently limited to the superficial structures, can usually be readily cured by the surface application of radium either in plaques or tubes. If the plaque is used, a full strength applicator, screened with 0.1 mm. of aluminum, should be used, and a total dose of four to five hours given in two or three sittings. Should tubes be used, a screen of 0.5 mm. of silver and 1.0 mm. of rubber is satisfactory, if from 40 to 50 millicurie hours are given to each square centimeter of surface. Since metastases are rarely seen in epitheliomas at this stage if efficiently treated in the first place, prophylactic treatment of the cervical glands is unnecessary, though they should be watched for some time after the initial lesion is treated.

The more extensive cases, in which the subcutaneous tissues are involved, require more strenuous therapy. In this clinical variety of lip cancer, proper surgical removal of the growth with dissection of the regional lymph nodes, even though they are not palpable, is usually satisfactory, but for a number of reasons it may be desirable to treat it with radium. For these cases, in addition to the surface treatment advised in the more superficial type, from two to eight bare tubes of emanation should be buried in the tumor. These tubes should be from 0.5 to 1 millicurie each. This combined method of treatment will practically always clear the original lesions. The lymph glands of the neck should be irradiated in every case of this type, either with the roentgen ray or with a suitable radium pack, whether the glands are palpable or not. If the roentgen ray is used, 60 milliampere minutes at a 10 inch distance, with a 10 inch spark gap and 5 mm. aluminum filter, should be applied to each of three areas every three or four weeks for three or four times. Should a radium pack be used, 3,000 to 4,000 millicurie hours at 3 cm., filtered through 2 mm. of lead, may be given each of three areas every four or five weeks for three or four times. Should palpable nodes be present at the outset they should be surgically removed a week or two after the first irradiation and the areas irradiated again subsequently. If metastatic nodes develop during treatment, radical removal is indicated.

Very extensive carcinomas of the lip, involving the greater part of the lip and with massive metastases are as hopeless under radiotherapy as under surgery. Some of these cases may receive some palliation, particularly in decreasing pain and in healing ulcerative areas. Massive doses of radium or roentgen ray do more harm than good and conservative therapy only is indicated.

Fig. 10.—Superficial basal-cell epithelioma of inner canthus; 10 mg. full strength plaque, 0.1 mm. aluminum, total four hours.

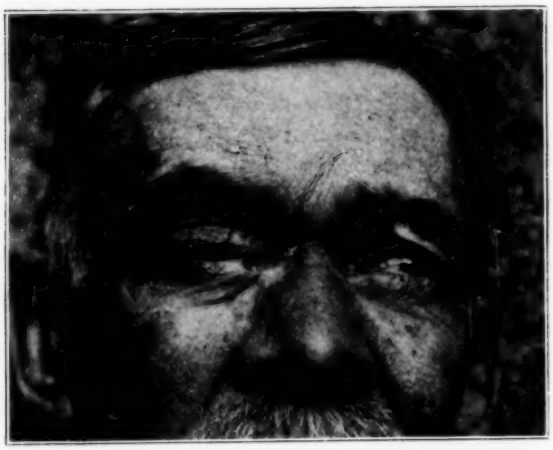

Fig. 11.—Epithelioma, basal-cell, of inner canthus. This appeared to be a superficial ulceration but proved to be a deep infiltration, involving the bone; five mg. half strength plaque, brass 0.3 mm., total five hours; one bare tube, 0.5 mc., buried into the mass; subsequent surgical removal of the sequestrum.

THE TWO TYPES

Aside from cornifying carcinoma of the lip and ear, these lesions may and do occur anywhere on the face. In general they conform to one of two types: (1) the mushroom or fungating type, and (2) the infiltrating type. These types are not at all distinct, and the one often merges into the other. In general, it may be said that when the fungating form predominates, metastases occur relatively late and the prognosis is therefore better. The infiltrating type may clinically resemble closely a rodent ulcer and when this occurs the only differentiating feature is the rapidity of growth. In these cases surgery is of value, but wide excision will be necessary for a cure. In treating them with radium, the most efficient possible radiation is imperative. Halfway measures are worse than useless. Cosmetic results cannot be thought of. Wherever possible, buried bare tubes of emanation should be employed, and this treatment augmented by the use of applicators on the surface. The lymph glands draining the area involved should be treated as outlined for epithelioma of the lip.

CONCLUSIONS

In the treatment of basal-cell carcinoma of the face it is seldom necessary to employ buried bare tubes. Surface application, except in the deeply infiltrated and very extensive cases, are usually satisfactory.

In the great majority of squamous-cell carcinomas, buried bare tubes used in conjunction with surface applications have been very helpful. In the radium treatment of deep carcinomatous infiltrations, buried bare tubes are almost a necessity.

ABSTRACT OF DISCUSSION

DR. HENRY H. HAZEN, Washington: It seems to me that the therapeutic action of radium and that of roentgen rays is practically identical. A few weeks ago I reported a series of over 100 cases of epithelioma treated by roentgen rays and followed to end-results. The results were very good. In these cases we had nineteen recurrences. Some of these were sent in for radium treatment after roentgenotherapy had failed; not in one instance was the cure affected by radium. We might also add that several of the patients had been treated by radium before they came to us for roentgenotherapy. Some of them were treated by a doctor who was a gynecologist, not a dermatologist, but in this series the radium showed no advantage over roentgenotherapy.

In regard to sequelae, in the cases with basal-cell growths which we handled, we found telangiectasis resulted in only seven cases, and the scarring was no more marked than in cases in which radium is used. There is one thing which is rather striking, and that is that when roentgen rays are used up to two or two and a half skin units in an area not over three fourths of an inch square, telangiectasis is not likely to result; but if a much larger dose is used on the same patient over a larger area telangiectasis may result. We do not, it seems to me, have more sequelae from roentgen therapy than from radium therapy.

In regard to the ear, we are in doubt about treating basal-cell carcinoma of the ear either with radium or with roentgen rays. We have found that they are not particularly effective in a large series of cases. It is our practice now to take these growths out with a cautery rather than to attempt removal with roentgen therapy.

I often wonder if in the use of radium and roentgen therapy we do not employ too heavy filtration. It is not unusual to see a case of prickle-cell or basal-cell carcinoma in which a heavy filtration has been used without response, treated only once or twice with a heavy, almost unfiltered ray, followed by good healing almost at once. The same thing is at times true in the cases of lymph nodes. I am sure we obtain better results in employing a rather light filter of aluminum, about 2 mm. instead of 5 mm.

Dr. August Ravogli, Cincinnati: I must emphasize the work that Dr. Morrow has shown us and must add also to the praise for radium. I have felt that in radium we have the ideal treatment for the superficial epithelioma of the skin. The great question, as Dr. Fox has said, is to have the technic standardized, and eliminate the alpha rays, which are irritating and produce a constant reaction without doing any good. We should use only the beta and gamma rays, and this work is done entirely by the screen. In my office, we use the silver and copper screen and also black paper, according to the depth of the epithelioma. I had a patient, referred to me by Dr. Carmichael, who had a large basal-cell carcinoma of the temporal region. I treated it by scraping, and burning and obtained a pretty good result; but the patient returned two years later with a big tumor, and was treated with radium. The tumor disappeared, leaving only a thin scar. Recently the patient returned with a small, ulcerating epithelioma in the center of the scar and has received two hours more of 50 mg. of radium. I do not know yet what the result will be, but surely we can say this is the ideal method for treating epithelioma.

Of course, when the glands are affected I believe surgical treatment is necessary, together with radium therapy. The radium dissolves and makes innocuous the cells which constitute the cancer. About two weeks after the application of radium, when the reaction starts, if a piece of the epithelioma is taken and examined microscopically, one finds no more of the epithelial cells, but only the connective-tissue cells which take the place of the old cancer cells, and in this way all the cancerous appearance is entirely gone.

I agree with Dr. Morrow that radium therapy for the epithelioma or superficial cancer of the skin is the ideal treatment, and we can congratulate ourselves that we have a means of relieving patients who were condemned to suffer.

Dr. Richard L. Sutton, Kansas City, Mo: On one or two points I differ with Dr. Morrow. In the treatment of carcinoma of the ear, my experience does not coincide with his. In cartilage involvement, we have found both radium and the roentgen rays of little use. Careful dissection gave us the best results.

In the treatment of simple, noncomplicated basal-cell carcinoma of the skin, curettage, followed by acid nitrate of mercury (as originally recommended by Sherwell), with radium later, gives the best cosmetic results and the best guarantee of a permanent cure. We have secured better results from the use of radium plaques in these cases than from tubes, probably because of the larger area treated when the plaques are employed. Short, oft repeated doses, have, in my hands, proved superior to single, long exposures. In other words,

ten or a dozen exposures, of one-half hour each, give better results than a single exposure of five or six hours. I am glad to learn that Dr. Morrow and Dr. Pusey have had the same experience.

In attacking cancer of the lip, cross firing, with plaques or with needles has given the best results in my hands.

Dr. Douglass W. Montgomery, San Francisco: There are possible explanations of the excellent results we get with carcinoma of the lip treated with radium. We now, in physiology, recognize five tissues instead of four—epithelial tissue, connective tissue, tissue of muscle, tissue of nerve, and in addition we regard blood as a tissue. Blood tissue happens to be the richest in metal. Only those rays of electromagnetic energy, however, which are absorbed are of value in the treatment of epithelioma, and we know that the presence of metal causes the absorption of those rays. Therefore, the probable reason why we get such brilliant results on the lip and on the eyelid is that, in these situations, there is a great deal of blood, with its heavy load of metal, causing the absorption of the electromagnetic energy.

I confess that the results we get in cancer of the lip now are astonishing to me. I never could get them with roentgen rays, but, of course, it may be that in my practice I never had attained to the expertness with roentgen rays that Dr. Pusey had. He showed results that we, in our office, could not attain. I do not know what the difference in technic was.

There is another point I wish to mention. It refers to the advantage of the split dosage, and there may be a physiologic reason for that also. Karyokinesis plays an important part in all malignant growths. Karyokinesis consists, first, in the complete disappearance of the nuclear membrane; then the cell contents, including the nuclear constituents, are scrambled; then two poles are formed, and around each pole a nucleus appears. Then nuclear membranes are formed and the cell divides into two parts, each with its nucleus, and so two cells are born. There is, therefore, a time in the division of the cell when the nucleus, the nub of the cell so far as vitality is concerned, is unprotected by its membrane and is sensitive to injuries as at no other time. Now, if the gamma rays hit that cell at the particular time, it is only fair to suppose that it will kill that cell much more readily than if it had a nuclear membrane.

As new cells are being formed continuously, an interrupted treatment would hit more of these sensitive cells than a continuous treatment. In other words, an interrupted treatment would be equivalent to fractional sterilization. This would indicate that fractional dosage is the best method to employ. In conversation, Dr. Pusey has said that the foregoing would explain why he, with interrupted dosage, gets better results than by continuous application.

These two points, I think, are exceedingly interesting in our treatment of these cases.

Dr. William Allen Pusey, Chicago: These papers on radium and the roentgen ray are always interesting, and I think we all are getting about the same results. I would call attention to the fact that I have been getting practically all the results with roentgen rays for at least twenty years. I have had radium for at least seventeen years and have used it in these cases, and have carefully tried to see some difference between the results; but I will reiterate what I have said before—that I can see no difference whatever, even as to the point of radium burn.

The point which Dr. Hazen brought up about telangiectasis in small areas and not in large, I think is explainable. When you produce a roentgen-ray scar you destroy most of the blood vessels and those that remain are enlarged

to compensate for those that are gone. If you have an area the size of a small coin, the amount of compensating hypertrophy is small, but if the area is as large as a foot, you get more telangiectasis. That to my mind is an explanation of what I think is a fact. My experience agrees with his as to telangiectasis.

As to the different kinds of results Dr. Morrow has obtained, they conform with mine. After a short experience I formulated this rule: I was willing to treat with roentgen rays any epithelioma, basal cell or squamous cell, which did not require the removal of adjacent glands or other deeper tissues. I have lived up to that rule ever since, according to my best judgment, and have had no reason to depart from it, or to believe it not a good rule. Very early in my experience, through some surgeon, I began to treat epithelioma of the lip. Patients with epithelioma down deep in the substance of the lip I do not wish to treat, but if there are superficial lesions involving some portion of the lip I am willing to treat them. The ex cathedra statement was often made that the treatment of epithelioma of the lip except by a surgeon was a crime. I have been doing it for twenty years, and I would be willing to put my results against anybody else's results. As a matter of fact, when you find carcinoma in the glands of the neck, surgery has nothing to hold up its head and be proud about.

About epithelioma of the eyelid: I have treated these for many years. I am willing to take the position that any one who treats an epithelioma of the lid by incision without considering radium or roentgen rays is not giving the patient his best chance. In the inner canthus the lesions are likely to go into the orbit, and when they do so treatment is of little avail. At the outer canthus I get better results. I have no difficulty in avoiding radium dermatitis about the lids.

About the ear, I do not see the trouble that Dr. Sutton spoke of. Of course if you have carcinoma where there is nothing but cartilage it heals slowly, but I treat these carcinomas with considerable success. I have plaques that are small enough to get down into the small folds and I secure good results.

Dr. Harold N. Cole, Cleveland: I just wish to mention a therapeutic suggestion. An article was published in the *Annals of Otology* about a year ago giving a method for protecting the eye by means of a brass ovoid that fits over the ball. Having filled the interpalpebral space with liquid petrolatum, one coats one of these ovoids with paraffin and slips it over the eyeball. Treatment can then be continued for an hour without effecting the eye. I secured one of these ovoids from V. Mueller and Company, Chicago, and think it is the finest thing that has ever been devised for protecting the eye during radiotherapy.

Dr. Henry H. Hazen, Washington: It has been the fashion recently for a large number of institutions to rent radium to people in the town. They form a company and secure a certain amount of radium which they rent. I believe one thing should be emphasized: Radium treatment cannot be standardized except by biologic tests. You cannot measure the millimeters and time and so forth, as with roentgen rays, and if a man goes to an institute and rents radium he will get into trouble at times. I think it should be emphasized that a physician cannot rent radium and obtain the same results that Dr. Pusey or Dr. Morrow can.

Dr. William Allen Pusey, Chicago: I have treated these cases for twenty years for surgeons and am sure some of them think it does well. There have been cases in which there have been nodules even in the armpit and the nodules have disappeared. I believe it can be established that you can get rid of many

carcinomatous glands in certain localities by means of roentgen therapy. I feel very doubtful about the efficiency of any technic in the neck, but in the axilla and breast I think the probability is strong that you can destroy those masses. I have seen some cases that seemed to leave no possible doubt that roentgen therapy had cured recurrent carcinoma that was inoperable. For example, I treated a woman, a physician, eighteen or nineteen years ago, who had a family history with more carcinoma in it than I had ever known, and who had had two and perhaps more operations for recurrences on the chest wall. There was nothing left except skin and ribs, but she had some recurrence in the axilla at that time and a little under the glands of the skin surface. With all her history and those recurrences, that woman still sends me some sort of memento every Christmas.

Dr. Howard Morrow, San Francisco: In regard to the subject of screening, two years ago I was inclined to think that we should use heavy screens and prolonged exposures, but little by little I have come to the conclusion that we want to screen less and use shorter exposures. I believe all applicators should be screened, certainly with rubber, and even in superficial cases should have at least 0.1 mm. of aluminum. In the deeper lesions we can use a longer time and screen with 0.2 mm. of aluminum. If a massive dose is necessary, we can screen with 0.5 mm. of silver and 0.1 mm. of rubber. Beyond that greater screening is seldom necessary in superficial lesions.

HYPOTHYROIDISM WITH UNUSUAL SKIN MANIFESTATIONS

REPORT OF A CASE *

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AND
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The case herewith reported presents features of such unusual interest that it seems to us worthy of record. The patient was a young child under our observation in the ward on three different occasions. Each time she was discharged as well. We have, however, been able to observe the evolution and involution of each attack from start to finish. The salient characteristics of the various attacks have been the same. The eruption, starting at a given point, would spread by the development of new lesions at a distance until it had become universal. In each attack the primary lesion was a purulent, subepidermal vesicopustule of pin-point size, which rapidly undermined the lower layers of the epidermis and finally broke through, leaving a jagged tear like that made by a rough-pointed stick pushed through a sheet of paper; marked redness and edematous swelling were present. A high temperature characterized the first two attacks, but not the third.

The history of the case follows:

History.—The mother was living and well. She had married twice. The patient was the child of the second husband, who was living and well. There were six children by the first husband, of whom three were living and well. There had been one premature birth. Two children died in infancy. The mother had been twice pregnant by the second husband. She had miscarried once in the third month. The patient was the second child. There was no history of skin disease or of malignant disease in the family. The patient was born at full term after a difficult but not an instrumental delivery. She was breast fed for two months, after which she was bottle fed. It had been difficult to regulate the food. In 1919 she had measles; in 1920, influenza, and a skin disease with a cervical abscess. Other acute infections were not admitted. She had had no accidents.

The only evidence of venereal disease was the fact that the mother had had two miscarriages (one by the first husband, one by the second).

There had been no objective symptoms of eye, ear, nose or throat trouble, and no cardiorespiratory diseases had been noted by the mother. The appetite was never good, and there was a tendency to constipation. There was enuresis persisting even to the present. The child was not able to sit straight at the age of 2 and not able to talk well even at the time of examination. There was evident mental retardation.

The patient slept well.

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* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

Fig. 1.—This photograph shows the dull facies, so characteristic of the early phases of this case and also the universal distribution of the eruption. After thyroid medication the "swollen" look of body and face cleared up and the skin became smooth and soft.

Physical Examination.—Examination on admission, July 20, 1920, revealed that the patient was well developed and well nourished. The skin was of pasty color. The child looked drawn and anemic. The only parts of the body not involved were the face, palms, soles and scattered areas on the legs. The rest of the body was a mass of dry, wrinkling, sloughing skin, which was puffed up in many little white areas suggestive of pustules. The course of a single lesion seemed to be as follows: Erythema appeared, in the center of which was a small whitish point which gradually increased in size until it joined with the whitish centers of neighboring lesions. This whitish center seemed to be due to air, for there was no exudate when one was opened. The process gradually undermined the skin until, after several lesions had coalesced, the entire area sloughed off. The sloughing seemed to be of the superficial layers of the skin only, and the process was possibly intradermal only. There was no bleeding, no excoriation or fissuring. The outer layers of skin rubbed off with slight pressure.

Examination of the internal organs and glands was negative. The thyroid gland was not enlarged and there were no unusual glands.

The child was backward in her development. She was 3 years old and could not talk. She was not active and did not want to play. The abdomen was large and protuberant. The patient had coarse dry hair and short, fat, chunky, pudgy hands and fingers, all of which was at least suggestive of some thyroid dyscrasia.

Treatment.—The chief medication was thyroid, one-fourth grain, three times a day, with various external applications, such as iodin and mercurial ointment.

Progress of the Disease.—In ten days the process had advanced to the toes, which were the last to be affected. The older portions dried and desquamated freely and newer advancing lesions continued to start, with swelling, redness and seropurulent exudate, undermining the epidermis. Where the process had healed, there was no evidence of recurrence of the vesicopustules.

Microscopic Examination.—July 20, examination of the blood revealed: leukocytes, 9,600; hemoglobin, 60 per cent.; polymorphonuclears, 37 per cent.; lymphocytes, 30 per cent.; large mononuclears, 20 per cent.; eosinophils, 3 per cent.; basophils, 1 per cent.; blasts, 9 per cent. The erythrocytes manifested some change in size and shape and some achromia.

July 21, examination of the urine revealed much squamous epithelium, amorphous phosphates and many long filaments like mycelia. Other streptococci and some long strings of bacilli were apparent.

The stools were negative. The Wassermann test was negative.

July 30, seven cultures were made from the vesicopustules on five different mediums. There was no growth on any.

Results of Treatment.—August 5, two weeks after admission, improvement had been remarkable. The process was no longer active. Now there was comparatively little scaling except on the legs. The skin was becoming soft and pliable. Simultaneously with the clearing up of the skin, the child became brighter, and no longer gave the impression of low mentality. The facial expression was one of progeria.

Consultations.—August 14, a nerve consultation revealed the knee jerk present; no clonus and no Babinski sign. The pupils were equal. The patient paid little or no attention to the voice (deaf?). She manifested retarded mental development. The condition suggests hypothyroidism.

August 16, an orthopedic consultation revealed congenital defects of the spine.

Course of the Disease.—August 16, the temperature rose suddenly to 105.6 F. without apparent cause. There was no increase in activity in the skin process. Enlarged tender reddened glands in the right supraclavicular fossa suggested the cause of the fever. There was no trouble elsewhere, either external or internal.

August 17, the von Pirquet reaction was negative in twenty-four and forty-eight hours.

Thyroid, one fourth of a grain, three times a day, was prescribed. Locally, paste 2 and wash 2, unguentum 13, were used. Paste 2 consists of crude coal tar, 2 gm.; zinc oxid, 2 gm.; pulverized starch, 15 gm.; petrolatum, 15 gm. Wash 2 consists of zinc oxid, 8 gm.; calamine, 4 gm.; phenol, 2 gm.; lime water, ad 250 c.c. Unguentum 13 consists of ichthyol, 2 gm.; precipitated sulphur, 2 gm.; petrolatum, 30 gm.

August 21, there was definite fluctuation in the enlarged glands and the child was discharged to the surgical ward for operation. At this time the skin was clear except for a few pustules about the swollen glands.

Fig. 2.—This photograph shows the same "swollen" look as in Figure 1. It also shows the extensive undermining and loosening of the epidermal layer from its attachments which characterized the acute, spreading phase of the eruption.

SECOND ADMISSION

History.—The child was admitted for a second time to the hospital on Feb. 8, 1921. Following her discharge from the hospital, August, 1920, she was in an institution. The thyroid medication was continued for a time until, owing to some intercurrent illness, it was thought advisable to stop it. Two weeks previous a fresh outbreak had appeared which resembled that of July, 1920.

Examination.—On admission it was noted that the child had lost her brightness, was indifferent, and had no interest in her surroundings. She could not be made to talk or play. Her face had grown broad and square and looked swollen. The eyes were set deeply in greatly bulging cheeks. The general aspect was that of a child of low mentality of the myxedematous type.

Over the external region, in the axillae and over the region of the shoulders, were large sheets of eruption. Elsewhere on the trunk were scattered lesions in moderate abundance. As in the preceding eruption, the outstanding features

were the reddened and swollen skin on which were seated groups of the eruptive lesions. The primary lesion resembled that of the previous eruption in that it was a minute, turbid vesicle which grew peripherally, and rapidly undermined and loosened the epidermis as it spread. By coalescence large areas became involved, and more and more regions were affected until the disease became universal.

The general aspect of the disease reminded one at once of an acute dermatitis exfoliativa in the swelling and redness, and of an impetigo herpitformis in the character and arrangement of the lesions. The undermining and loosening of the epidermal layer was like that seen in pemphigus foliaceous.

The urine has remained negative. Blood as at first examination, July 20, 1920. The Wassermann reaction was negative. Smears and cultures from the purulent lesions were entirely negative on all occasions.

Course and Outcome.—As before, the acute stage of the eruption was accompanied by a temperature running as high as 105 F. on several occasions. After three or four weeks the temperature returned to normal.

The course of the disease was comparatively rapid, the child being dismissed March 5 with almost no scaling and no trace of the previous eruption.

The most striking feature of the case was the rapid transformation in the child's mentality and general aspect after the administration of the thyroid.

The first test of her basal metabolism revealed a deficiency of 19 per cent. Consequently, the dose was increased from one fourth of a grain three times a day to 1 grain three times a day. Within a week, the change in the mentality and in the skin was noticeable. Two weeks later, the child was playing and talking, and the skin was almost cleared. The second test made March 2, 1921, showed a deficiency of 5.4 per cent.

Prior to the administration of the thyroid, various applications had been tried, but without effect.

THIRD ADMISSION

In May, 1921, the child was admitted to the hospital for the third time. On this occasion the eruption lacked the former symptoms of swelling and bright redness which had characterized the two preceding attacks. Over the trunk, front and back, was an eruption which partook in part of the characteristics of acute psoriasis and of acute seborrheic eczema. There was no longer a tendency to undermine the skin.

The course of the disease was shorter than before, ending in three weeks. As in the previous attacks, the process became practically universal. The most striking feature was the general exfoliation of the epidermis in large tissue-paper-like flakes. The child's general condition was good. She was bright and playful, although her mentality was still below par.

ABSTRACT OF DISCUSSION

Dr. E. L. Oliver, Boston: The case was exceedingly interesting to me, as I was able to watch it through the three attacks. I think any one would recognize it as a case of hypothyroidism, but there are very few cases of pustular eruption occurring in hypothyroidism. In 1919, Hudelo published an article on a vesicular bullous eruption associated with hypothyroidism; but, so far as I know, this is the only case that has been associated with this disorder. At the time of the last admission to the hospital, we were advised by the pediatrist against giving thyroid, but if we had not given it I feel sure the eruption would have continued to increase. We gave the thyroid, increasing the dose to 7½ grains a day, and the eruption disappeared much more rapidly than on 3 grains

a day. I think the child needed thyroid, despite the test of the pediatrist. Science has not yet concluded what the normal metabolism is for a child of that age. I think we must be guided by the symptoms and use thyroid more or less empirically, in spite of what the pediatrist says in cases like this.

Dr. Ernest L. McEwen, Chicago: I should like to know what the orthopedist's decision was about the back, and if there was any tuberculous element in the condition in the neck.

Dr. August Ravogli, Cincinnati: The eruption looked to me like a form of lichen scrofulosorum, accompanied by a kyphosis. I think the lichen scrofulosorum was probably produced by tuberculosis.

Dr. Harvey P. Towle, Boston: One of the interesting points about this case to me was that it was my first introduction to the measurement of thyroid therapy by an attempt at an accurate measurement of metabolism. We were giving the child one fourth of a grain, three times a day, which I thought was a fair dose. This was increased to 1 grain three times a day, which the child stood well. The result was interesting, for the test now showed a deficiency of only 5 per cent., whereas it had previously given a minus 19 reading. This parallel response seems to indicate that the test may become very valuable. As Dr. Oliver said, the normal limits of the thyroid metabolism have not been worked out.

As to the abscess in the neck, there was no question of tuberculosis. It was a straight coccus infection which developed rapidly and healed promptly after surgical measures.

As to lichen scrofulosorum, had Dr. Ravogli seen the case early there would have been no question of that.

The orthopedist does not consider the deformity of the back due to tuberculosis. There was scoliosis and kyphosis, but no question of any tuberculous process.

THE FATTY ACIDS OF CHAULMOOGRA OIL IN THE TREATMENT OF LEPROSY AND OTHER DISEASES

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Since my original publication,[1] much interest has arisen as to the value of these fatty acids in leprosy and other diseases, especially tuberculosis.

On reviewing the literature on the use of the oil by subcutaneous injections, I find that it was probably first used by Blanc of New Orleans as early as 1888, according to Dyer.[2]

Sandes [3] has also used it hypodermically at Robbins Island. Black [4] gave a mixture of olive oil and chaulmoogra oil.

Ohmann-Dumesnil [5] gives preference to the hypodermic administration of the oil.

Jeanselme,[6] in 1911, published the formula which was probably the basis of the Mercardo formula employed later in the Philippines. It was composed of chaulmoogra oil, guaiacol and camphor.

Tourtoulis [7] read a paper before the Academy of Medicine of Paris on several years' experience in the use of the oil subcutaneously.

Miguel [8] and Unna [9] both report good results from the use of the oil subcutaneously.

More recently Mercardo,[10] in the Philippines, obtained such excellent results that renewed attempts were made with the oil subcutaneously, and further experiments were encouraged, notably those of Sir Leonard Rogers in India and my own in Hawaii.

The chemical composition of chaulmoogra oil was first investigated by Powers and Gornall in 1904. They isolated a new series of fatty acids, among which were chaulmoogric acid ($C_{18}H_{32}O_2$) and hydnocarpic acid ($C_{16}H_{28}O_2$).

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1. Hollmann, Harry T.: Chaulmoogra Oil in Leprosy, J. Cutan. Dis. **37**: 367 (June) 1919.
2. Dyer: Am. J. Trop. Dis. **2**:295.
3. Sandes: J. Trop. Med. **15**:65.
4. Black: Lancet, April 28, 1906, p. 1167.
5. Ohmann-Dumesnil, A. H.: The Treatment of Leprosy, J. A. M. A. **40**: 1351 (May 16) 1903.
6. Jeanselme: Presse méd., 1911, No. 96, p. 989.
7. Tourtoulis: Lepra **2**:107.
8. Miguel: Lepra **2**:120.
9. Unna: Arch. f. Dermat. u. Syph. **105**:299.
10. Mercardo: Pub. Health Rep., Supp. 20 (Oct. 16) 1914.

In 1916, Dr. Sudhamony Ghosh [11] working in India on this problem, isolated seven fractions of fatty acids from chaulmoogra oil by a method of fractional crystallization. These were converted into sodium salts and used by Sir Leonard Rogers in the treatment of leprosy.

The results of Sir Leonard Rogers' work [12] is that in 40 per cent. of fifty-one patients treated the lesions completely disappeared.

About the time that Rogers and Ghosh were starting their investigations in India, in Hawaii I interested Miss Alice Ball, M.S., an instructress in chemistry at the College of Hawaii in the chemical problem of obtaining for me the active agents in the oil of chaulmoogra.

After a great amount of experimental work, Miss Ball solved the problem for me by making the ethyl esters of the fatty acids found in chaulmoogra oil, employing the technic herewith described:

BALL'S METHOD OF MAKING ETHYL ESTERS OF THE FATTY ACIDS OF CHAULMOOGRA OIL

The oil has been separated into four fractions by the following procedure, using 200 gm. of oil, or multiples thereof, at one time:

The 200 gm. of oil are saponified with alcoholic potash and the bulk of the alcohol subsequently distilled off. The potassium soap is poured into a considerable volume of water and acidified with hydrochloric acid. The fatty acids thus separated are washed with hot water, dried and dissolved in 450 c.c. of 92 per cent. alcohol. On standing overnight in the refrigerator, a large amount of fatty acid crystallizes out and is removed by filtration. From this first crop of crystals, by successive recrystallizations from alcohol, chaulmoogric acid is obtained. This is converted into the ethyl ester and forms Preparation A. The mother liquors from the successive recrystallizations of chaulmoogric acid, which contain all of the solid fatty acids which separated in the initial crystallization from alcohol, except the chaulmoogric acid recovered in A, are united and evaporated. The residue of solid acids is then esterified, forming Preparation B.

The filtrate from the initial separation from alcohol contains the acids which are more soluble in that solvent. These are converted into their lead soaps by first making the potassium soaps and then precipitating them with lead acetate. The lead soaps, dried either in vacuo or by repeatedly evaporating them down with alcohol on the water bath, are placed in 1,000 c. c. of ether. After thorough shaking, the mixture is allowed to stand overnight and the insoluble residue removed by filtration. These insoluble lead soaps, and the soluble

11. Ghosh: Indian J. M. Res. **4**:691 (April) 1917.

12. Rogers: Report of a Conference on the Leprosy Problem in India, 1920, Indian M. Gaz. **55**:125 (April) 1920.

portion recovered from the ether solution, are separately decomposed by treatment in hot water, with successive portions of acetic acid followed by hydrochloric acid. In this manner the lead is all removed and two portions of fatty acids recovered, differing from each other in the solubility of their lead salts in ether. These fractions are then esterified, yielding Preparation C from the fraction with soluble lead salts and Preparation D from that with insoluble lead soaps.

The four fractions are therefore:

(*a*) Ethyl ester of chaulmoogric acid.

(*b*) Ethyl esters of acids crystallizing from alcohol with chaulmoogric acid in the initial separation.

(*c*) Ethyl esters of acids soluble in 92 per cent. alcohol in first separation and which form ether soluble lead salts.

(*d*) Ethyl esters of acids forming lead salts insoluble in ether.

Sir Leonard Rogers [12] has followed out this line of work further and has used the sodium salts of the fatty acids of cod liver oil. In twenty cases, all patients improved, and in five all lesions disappeared.

Dr. E. Muir [13] reports that of 117 cases treated with sodium morrhuate, 71 per cent. manifested some measure of improvement, while 31 per cent. showed much improvement; and with the chaulmoogric sodium salt 132 cases, or 72 per cent., showed improvement and fifty-eight cases, or 32 per cent., showed marked improvement.

He says further that, from his experience, sodium morrhuate is as good as the sodium salt from chaulmoogra oil, and it has the advantage that it may be injected directly into the leprous nodules.

E. F. Neve [14] gives the results of treatment with both chaulmoogra and cod liver oil fatty acid sodium salts. He thus tabulates the results:

Gynocardate (chaulmoogra) treatment: much improved two, 10 per cent.; improved seven, 35 per cent.; not improved eleven, 55 per cent.

Morrhuate treatment: much improved two, 10 per cent.; improved six, 30 per cent.; not improved twelve, 60 per cent.

In his conclusions, he makes a pertinent remark: "Only about 10 per cent. show fresh manifestations of the disease while under treatment, some of which have been due to freeing of toxins by overaction of the drug."

The latter fact I also have observed in a number of cases under treatment with the ethyl esters of the fatty acids of chaulmoogra oil.

At times the ethyl esters will cause, in some of the cases, an apparent fresh manifestation of the disease; yet I am convinced, from the subsequent progress of these cases, that it is not a fresh manifestation of the disease, but an inflammatory reaction in previously unrecognized foci of the disease.

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13. Muir: Indian M. Gaz. **55**:139 (April) 1920.
14. Neve: Indian M. Gaz. **55**:128 (April) 1920.

McDonald and Dean [15] report that, in the use of the ethyl esters of the fatty acids of chaulmoogra oil in leprosy, they took the ethyl esters as isolated for me by Miss Ball and distilled them in vacuo at a pressure of from 30 to 34 mm. The distillate was cut into three fractions of different boiling ranges and was colorless. They say that the methods employed in their production did not result in the destruction of the therapeutic agent or agents.

I cannot see that there is any improvement whatsoever over the original technic as worked out by Miss Ball. The original method will allow any physician in any asylum for lepers in the world, with a little study, to isolate and use the ethyl esters of chaulmoogra fatty acids in treating his cases, while the complicated distillation in vacuo will require very delicate, and not always obtainable, apparatus.

McDonald and Dean report that of 186 patients under treatment during a period of fifteen months, 25 per cent. became bacteriologically negative. Unfortunately, they do not give any data as to the length of time these patients were under treatment. In their conclusions they say: "When combined with iodin, the fatty acids of chaulmoogra oil, and their esters, give good results; but there is no adequate proof that this addition of iodin causes any increase in the effectiveness of the material used."

Walker and Sweeney [16] summarize the results of their experiments in the bactericidal action of the fatty acids of chaulmoogra oil thus: "Chaulmoogra oil contains bactericidal substances that are about 100 times more active than phenol. The bactericidally active substances of chaulmoogra oil are the fatty acids of the chaulmoogric series, chaulmoogric and hydnocarpic acids, and possibly lower isomers of this series. The bactericidal activity of the chaulmoogric acid series is specific for the acid-fast group of bacteria and inactive against all other bacteria tested."

RESULTS OF TREATMENT

Since the establishment of the treatment of leprosy by the ethyl esters of chaulmoogra oil by me at the leprosy hospital (Kalihi Hospital), United States Public Health Service, Honolulu, eighty-four patients who have been on the treatment for periods ranging from four years to three months, have become bacteriologically negative and free from all lesions of the disease and have been discharged from segregation (paroled). These patients, before being paroled, were examined by a board of three medical men, whose duty it was to recommend whether or not the patients should be paroled from segregation.

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15. McDonald and Dean: Pub. Health Rep. **35**:1959 (Aug. 20) 1920.
16. Walker and Sweeney: J. Infect. Dis. **26**:238 (March) 1920.

Of the eighty-four patients, thirteen were under treatment less than six months; twenty-eight from six months to one year; thirty-six from one year to two years; five from two years to three years, and two from three years to four years. It will be seen that 76 per cent. of the patients were under treatment for a period ranging from six months to two years.

Of the eighty-four patients thirty-six were male, twenty-five having nodular leprosy, and eleven anesthetic leprosy. Forty-eight were female, thirty-five having nodular leprosy, and thirteen anesthetic leprosy.

It will, therefore, be evident to any one that of these eighty-four patients that have been paroled, at least sixty (having nodular leprosy) gave a bacteriologically positive reaction at the time of beginning treatment, and if reaction became negative under treatment and the patients were free from lesions, it is positive and undisputable evidence that the ethyl esters of chaulmoogric fatty acids, as isolated by Miss Ball for my use in treating leprosy, are capable when administered to patients with leprosy, of causing the disappearance of the lesions and the leper bacilli.

STAGE OF THE DISEASE AT THE BEGINNING OF TREATMENT

From the history obtainable from these patients, it was learned that twenty-one had shown evidence of the disease for only six months; thirteen from six months to one year; sixteen from one year to two years; eleven from two to three years; six from three to four years; five from four to five years, and twelve for more than five years. Of the eighty-four patients treated, and becoming free from all evidence of the disease, twenty-one had incipient cases (under six months); forty moderately advanced (from six months to three years); twenty-three advanced cases of leprosy (existence for more than three years).

From a careful study of the relation of the stage of the disease and the length of the time of treatment, it became evident that there was no relation between the stage of the disease and the length of treatment as many of the patients suffering from advanced cases gave a bacteriologically negative reaction as soon as some of the patients in the incipient stages. This is explainable, on the grounds that many of the patients having advanced cases have already produced within themselves certain protective or curative agents which need only assistance from without to eradicate the disease from the body.

ETHYL ESTERS OF THE FATTY ACIDS OF CHAULMOOGRA OIL IN TUBERCULOSIS

I have treated only two patients with tuberculosis with the ethyl esters as isolated according to Miss Ball's technic. For use in these cases I prepare the esters thus:

1. One hundred and twelve gm. of caustic potash is placed in a flask and 1 liter of 95 per cent. alcohol is added. The mixture is shaken frequently until the potash is dissolved.

2. The alcoholic potash is poured into a second flask containing 400 gm. of chaulmoogra oil. The second flask and contents are placed in a hot water bath and a reflux condenser is connected with the mouth of the flask. The water in the bath is allowed to boil about one hour, being watched closely so that it (the waterbath) does not boil dry and that the alcoholic potash oil mixture does not boil up into the condenser. It is well to wrap a wet towel around the upper part of the flask in order to keep it as hot as possible. Should the mixture become too hot and start to accumulate in the condenser, the light should be lowered or turned out, and a cold wet towel should be wrapped around the flask in place of a dry one.

The water running through the condenser condenses the alcohol as it enters the middle tube of the condenser and it drops back into the flask.

The cold running water should enter the condenser through the lower end and leave through the upper one.

3. The light is turned out under the water bath and the reflux condenser is removed from the top of the flask. A bent glass tube is inserted in a rubber cork into the mouth of the flask. The other end of the bent tube is connected with the larger end of the reflux condenser by means of a rubber cork. The reflux condenser is slanted so that the smaller end is lower than the larger end and a second flask is placed under the smaller end of the reflux condenser.

The hot water bath is heated, and the alcohol that is condensed in the reflux condenser will now pass through into the second flask instead of dropping back into the first flask as previously.

Heating the water bath and distilling off the alcohol is continued until the alcohol drops very slowly into the second flask. All the alcohol cannot be distilled off, but it can be distilled off until the soapy substance in the first flask is quite thick.

While this fluid soapy mixture in the flask is still hot, it is poured into a large volume of water and shaken well several times. It is then acidified with chemically pure hydrochloric acid until it is acid to litmus. This makes a fatty acid of the soapy mixture. It will now begin to separate, fatty globules of a dark brown color rising to the top of the mixture.

To aid the separation, three or four tablespoonfuls of common salt is added and the mixture shaken well. After there is a clear separation of the acid to the top, as much as possible of the liquid below is drawn off.

The fatty acid mixture is washed with plain boiling water at least three times. The last time the mixture will have to be put in a separatory funnel to remove all the water.

4. The fatty acid mixture is dissolved in absolute alcohol in an amount sufficient for the purpose. The alcohol fatty acid mixture is boiled on the hot plate with hydrochloric acid gas passing through (an operation consuming from forty minutes to one hour) until there is a separation in the flask. The ester is a muggy brown on top, and the lower layer is the alcohol.[17]

5. The whole content of the flask (ester and alcohol) is added to a large volume of water in a separatory funnel, while it is still hot, to remove the

17. For details of esterification, consult any analytic chemistry.

alcohol and hydrochloric acid. Some common salt is added to further the separation. It is allowed to stand over night, in order to obtain a clear separation.

The lower layer is poured off leaving the layer of ethyl ester in the separatory funnel. The ethyl ester is dissolved in the separatory funnel with ether. About a handful of calcium chlorid is added to the ethyl ester, and it is corked and shaken well. It is then allowed to stand twenty-four hours. This removes all the water. It is then drawn off from the separatory funnel into a clean separatory funnel, leaving the calcium chlorid in the first funnel.

A flask is placed on an electric hot plate and the ethyl ester is allowed to drop into it, drop by drop through filter paper. This evaporates the ether.

The product is now ready for use. It does not need to be sterilized.

CASES TREATED

In an advanced case of pulmonary and intestinal tuberculosis, the patient received ten weekly injections of 2 c. c. each without improvement.

In a case of incipient tuberculosis, with bacilli in the sputum, the roentgen ray showing involvement of the apex, the patient has so far received twelve injections of the ethyl ester, totaling 14 c. c. There has been a cessation of all cough, an increase of 15 pounds in weight and disappearance of night sweats. As there has been no expectoration it has been impossible to examine for bacilli.

I have treated two patients with lupus vulgaris of the face with small doses of the ethyl esters injected directly into the lesions, with complete disappearance of the lesions in one case and great improvement in the other. One drop was the amount injected into each lesion. The injections caused a marked erythema of the lesion, which lasted about ten days, and was followed by retrogression of the lesion. The injection was repeated as soon as the reaction had passed.

In one case of psoriasis I have given the patient fifteen injections, totaling 40 c. c., with no results.

SUMMARY

The fatty acids of chaulmoogra oil are bactericidal for the acid-fast group of bacteria [16] and cause the lesions and bacilli to disappear when administered to lepers, either in the form of the sodium salt [12] or the ethyl ester.[1]

It is too early to say that in the fatty acids of chaulmoogra oil we have a cure for leprosy. The patients who have become free from all lesions and give a bacteriologically negative reaction should be under observation for a much longer period before making such a statement, although a number of the patients have been under observation for three years or longer (those recorded in my preliminary report) after parolment, with, so far as I know, no return of the symptoms of the disease.

CONCLUSIONS

1. We have in the fatty acids of chaulmoogra oil, either in the form of the sodium salt [12] or in the ethyl ester,[1] a remedial agent that will cause a disappearance of the leper bacilli and the lesions of the disease, if administered over a sufficiently long period.

2. All patients who give a bacteriologically negative reaction should continue under observation and treatment for at least two years more.

3. From the results obtained in two cases of lupus, the ethyl esters of chaulmoogra oil fatty acids should be given a trial in cases of this disease, as well as in other forms of tuberculosis.

LICHEN PLANUS ET ACUMINATUS ATROPHICANS

LICHEN PLAN ATROPHICUS, LICHEN PLAN SCLEREUX, HALLOPEAU; LICHEN RUBER PLANUS KELOIDIFORMIS, PAWLOW; LICHEN PLANUS MORPHOEICUS, CROCKER; LICHEN ALBUS, ZUMBUSH *

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It has been my good fortune to be able to report this extremely rare and interesting case. The rarity of the disease and the multiform character of the lesions are of sufficient interest in themselves. In addition, the case serves as a corroboration to one of the conclusions reached in a previous article,[1] namely, that lichen planus and lichen acuminatus are closely related to one another. One of the arguments on which this conclusion is based is the comparative frequency with which the two diseases occur at the same time in the same person.

There are a number of cases on record that have points in common with this one, but after diligently searching the records, I fail to find a single case that corresponds to it in all particulars.

Dermatology is extremely rich in names. The rarer diseases especially have each been described under several headings. Many writers believe that they are describing diseases hitherto unknown and coin new names for them. For that reason I hesitate before giving this article its title, which expresses briefly the clinical and pathologic findings of the case, and I hope that, some day, this group of rare cases will be properly classified. The case is one of the rare modifications of lichen, namely, the atrophic form, with the difference that, to the lesions of atrophic lichen planus (Hallopeau) are added those of lichen acuminatus.

There is a certain degree of confusion in the meager literature of lichen atrophicus.[2] There are a number of cases reported in which the lesion consists of an atrophic central patch with a pink, red, violaceous, or brown border. In others, the central patch is white, hard, and parchment-like, while in still others the skin, although depigmented, is

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1. Feldman: Lichen Acuminatus, J. Cutan. Dis. **37**:226 (April) 1919.

2. A complete bibliography of the literature of lichen atrophicus up to the year 1910 will be found in Ormsby's article, Lichen Planus Sclerosus et Atrophicus (Hallopeau), J. A. M. A. **55**:901 (Sept. 10) 1910.

normal. Then, again, there are cases on record in which the lesion is a papule as large as a pinhead or a pea, pale or white, flat and angular, or raised and globular, rounded or irregular, with or without a pink or a red border. The papules in these cases are described as possessing one or more horny plugs, comedo-like bodies, or dilated follicles, while others lack them entirely. Some cases, with lesions widely differing from one another, have been described under one name, while similar cases have been described under a long list of different names.

HISTORICAL

Morand Baker had a case, in 1882, in which the papules were white and were surrounded by fine blood vessels. At times they had a linear arrangement. When they were grouped, the surface looked wrinkled.

Hallopeau reported four cases, the first in 1887.[3] In this case there were white shiny papules and patches, with deep central depressions representing dilated follicles and sweat gland ducts. The patches formed were white, shiny, scar-like, and itching. He, at first, named the condition lichen atrophicus, but after the pathologic findings of Darier[4]—atrophy of the papillae, fibrosis and infiltration of the corium, and dilated follicles and sweat gland ducts—he renamed it lichen sclereux when he reported his next case, in 1889.[5] In this patient the papules were white from the start, and Hallopeau, therefore, thought that this condition was not a modification of lichen planus, but an entirely new disease. He, however, modified this view, when, in 1896, he reported his third case,[6] in which distinct and typical lichen planus papules were present, as well as distinct lichen planus lesions in the mouth. He then came to regard this condition as one of the variations of lichen planus. The young lesions, in this case, were pale papules and patches with rose-colored or violaceous borders resembling morphea. The older lesions were large, depigmented patches with a pigmented zone at the periphery of each and with outlying typical lichen planus papules. One of the patches was exceptionally large, its dimensions being 34 by 17 mm. (1⅓ by⅔ inches). There were also papules that resembled the ones described, but they had pale centers with central depressions or comedo-like bodies. The fourth case was reported in 1898.[7]

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3. Hallopeau: Lichen plan atrophique, Union Med., 1887.

4. Darier: Lichen plan sclereux, Ann. de dermat. et .syph. 1892, p. 833.

5. Hallopeau: Lichen plan sclereux, Ann. de dermat. et syph. 1889, p. 447.

6. Hallopeau: Sur un nouveau de lichen plan sclereux, Ann. de dermat. et syph., 1896, p. 57.

7. Hallopeau: Sun un nouveaus cas de lichen Wilson sclereux, Ann. de dermat. et syph., 1898, p. 358.

Zarubin [8] reported two cases. In one there were sharply outlined annular patches, also segments of rings and straight lines. They were slightly infiltrated and reddish-brown in color. There was a slight scaliness on the surface. The central patch within the annular lesion was made up of rose-colored papules confluent into a patch with depigmentation and real atrophy. Typical lichen planus lesions were found at the periphery. In the second case, the annular and serpiginous patches were red to reddish-brown, raised from the surface and infiltrated. The surface was waxy and shiny, and was thrown into folds. The central patch was white and atrophic and even scar-like. The outline of the individual papule was retained in the central patch in the form of a network. There were typical lichen planus lesions at the periphery, as well as white and shiny patches on the buccal mucosa.

Schwimmer's case,[9] reported in 1895, had the appearance of a generalized eczema, and only after careful searching lichen planus papules with horny plugs and comedo-like bodies were found.

In Crocker's case,[10] the papules were white, hard, flat, and angular, with a little pit or comedo-like body in the center. They were surrounded by a lilac rim, like morphea. Crocker states that the papules may run together to form a patch, but the outline of the individual papule is never lost.

Hoffman [11] reports a case in which there were large depigmented patches surrounded by a narrow, reddish rim with outlying small papules. The center of each papule was pale and at times atrophic. It was covered with an adherent scale or it possessed a comedo-like body or a small pit which was occasionally pigmented. There were typical lichen planus papules in the vicinity of the lesions. The depigmented patch had a porcelain-like appearance. A similar case was reported by V. Zumbush,[12] and he named it lichen albus.

Csillag [13] describes a case in which the papules were pale violet-red or chalky white. They were round or polygonal, globular or flat, or even depressed, each with a depressed center and a reddish rim. In the patches formed, the individual papule was plainly distinguishable.

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8. Zarubin: Ein Fall von Lichen atrophicus, Arch. f. Dermat. u. Syph. **51**: 306, 1900; Ueber atrophische und serpigenese Formen der Lichen ruber planus, Arch. f. Dermat. u. Syph. **58**:323, 1901.

9. Schwimmer: Lichen ruber planus atrophicus, Arch. f. Dermat. u. Syph. **33**:451, 1895.

10. Crocker: Lichen Planus, Its Variations, Limitations and Imitations, Brit. J. Dermat. **12**:421.

11. Hoffman: Ueber einen mehrere Jahren hindurch beobachteten Fall von Lichen sclerosus, Ikonog. Dermat. Fasc. **4**:153.

12. V. Zumbush: Lichen albus, Arch. f. Dermat. u. Syph. **82**:339, 1906.

13. Csillag: Dermatitis lichenoides chronica atrophicans, Ikonog. Dermat. Fasc. **4**:147.

There was a pale violet rim around each patch. There were horny plugs and, in places, also thickly adherent scales. He was able to follow the development of the lesion and says that there is at first a red, conical papule with a horny plug. In some cases, the papule becomes pale, the plug falls out, and the papule disappears, leaving a brown pigmentation, while in others the papule becomes pale and centrally depressed. It enlarges and joins others to form a patch.

In Reiss' case,[14] there were vitiligo patches with horny plugs and little pits and the patches were surrounded by sepia brown borders. It is more than likely that these borders were originally patches of lichen planus which cleared up and left the deep pigmentation behind.

Ormsby, in 1910, reported a series of six cases,[2] one of which was a new one. In all these cases there were either white, flat papules with comedo-like bodies, some of which were surrounded by a pinkish border, or there were white, occasionally atrophic and depressed patches in which the outline of the original papule was retained. In two of the six cases there were typical lichen planus papules present and, in spite of that, Ormsby says that the papule is never red at the beginning, that the white papule is primary, and that the disease is not a modification of lichen planus, but an entirely different condition. His pathologic findings agree with those of Darier, except that he found the infiltration in the lower layer of the cutis instead of in the middle layer, as described by the latter author.

Riecke[15] thinks that the lesion may develop from either a white papule or a typical lichen papule. The patch formed is not always white; it may be gray, brownish or red.

Hallopeau and Laredde[16] collected and described a group of cases under the name of tropho neurose dyschromique et lichenoides. All cases in this group were not unlike those described under the name of lichen atrophicus. Some of them even had the same pathology; but they all lacked the horny plug or the dilated follicle. There were three types described: (1) The Neuser type, in which the pathologic findings are the same as in lichen planus, but the papules are strictly localized within the patch of vitiligo and the follicular dilatations are absent; (2) the Rille type, in which the papules look like lichen, but the vitiligo patch is partly atrophic, and Rille considers it an erythema with atrophy; (3) the Hallopeau and Larat type, in which there is a central depigmented patch with peripheral hyperpigmentation and lichenoid papules, but without horny plugs or dilated follicles.

14. Reiss: Uber atrophische Formen des Lichen planus, Arch. f. Dermat. u. Syph. **68**:137, 1903.

15. Riecke: Zur Kentnisse der Weissfleckenerkrankung, Arch. f. Dermat. u. Syph. **99**:181, 1909.

16. Hallopeau and Leredde: Traite pratique de Dermatologie, Paris, 1900, p. 793.

Pathology of the Depigmented Patch.—There is a hyperkeratosis, but no parakeratosis. Horny plugs project into the follicle and into the sweat gland duct. The stratum lucidum is absent. The stratum granulosum may be normal (Darier), diminished (Reiss), or missing altogether (Zarubin). Stratum malpighii is diminished and may be missing altogether. The papillae are flattened or they may be completely missing near the center of the lesion. Near the periphery they may be enlarged. Darier divides the corium into three layers. In the upper layer the fibrous tissue predominates. The bundles are packed close to one another and the cellular element is sparsely present. According to Reiss and Zarubin, infiltration is present in this layer and may even reach the stratum malpighii. The capillaries are either dilated or blocked. The elastic fibers are very fine and few in number. The middle layer consists chiefly of infiltrate. The greatest number of cells, composing the infiltrate, are small lymphocytes. There are also a few plasma cells and an occasional mast cell. Many young fibroblasts are present. In the third layer, the infiltration is localized about the vessels and glands.

REPORT OF CASE

History.—Mrs. S. S., aged 45, who had been married eight years, but had never been pregnant, had had her menopause three years previously. About two years previously her husband disappeared from home and was found later wandering in a semidemented condition. His case was diagnosed as one of advanced paresis. In November, 1918, the patient began to experience an itching and burning sensation of the face and of both forearms. Within a month, little patches appeared on the forearms and on both sides of the face. A few weeks later, the patches in the former region became ring-shaped, with a more or less clear center. They gradually increased in size to about three quarters of an inch (1.9 cm.) in diameter. About Feb. 1, 1919, she went to a dispensary for treatment, and there her case was diagnosed as ringworm. She received one or two treatments, and then she was told not to call again, as the disease would surely disappear if she continued using, a little while longer, the salve that had been given to her. The lesions, instead of improving, became larger and the itching increased. The lesions began to spread upward, reaching the arms by the end of March, at which time the patient went to another dispensary. There her case was diagnosed as syphilis, presumably on the strength of her husband's paresis. No blood test was made, but she received antisyphilitic treatment, which consisted mainly of mercury injections, She also received three arsphenamin injections, the last one just before she left the dispensary in August. Had the treatment been reversed, that is, had the patient been treated mainly with arsphenamin injections, there might not have been anything left for me to report. In June, while the patient was excessively overheated, she experienced a furious itching of the neck and the upper portion of the chest and shoulders. She states that there was no change in the appearance of the skin for about two weeks, after which time little red "pimples" appeared on the neck, upper portion of the chest, shoulders and both arms. She began to feel weak, and states that she lost 15 pounds (6.8 kg.) during the time she received the antisyphilitic treatment. There

was no relief from the itching, except for a short time immediately after an arsphenamin treatment. The slight benefit derived from the treatment was counterbalanced by reactions. She was annoyed by severe itching, and suffered from sleeplessness, weakness, and lack of appetite. Finally a blood examination was made, and the Wassermann reaction proved negative. When the patient was told that she was not syphilitic, she left the second dispensary and came to seek advice at Cornell.

Examination (Aug. 19, 1919).—The patient was a tall, well built, highly neurotic woman, who intelligently described her condition. She looked somewhat pale and slightly emaciated, and complained of weakness, nervousness, and lack of sleep, due to the itching.

On the back of the neck, in the region between the seventh cervical vertebra, the hair line, the mastoid bones, and the line of the sternocleidomastoid muscles, there were four large, annular and gyrate patches. The latter were thickened and elevated; the surface was smooth and shiny and violaceous in color. The normal skin lines were deeply marked. There was no scaliness. Close to the outer border of each patch were a number of typical lichen planus papules, each with a waxy surface and depressed center. The more or less circular area of skin enclosed within each patch was paler than normal, owing to a diminished amount of pigment. The color was not white, but a light pink. A large number of conical and pointed papules projected from the surface of each depigmented patch. The papules were pink or rose-colored and from the apex of each projected a fine filiform horny plug, which pulled out readily, leaving an almost colorless minute elevation with a central depression in its place. Most of the plugs were gray. A few of them, however, were short and black, and they resembled a comedo. Where the plugs had fallen out, there were minute pits. The papules in this location had a tendency to be arranged in parallel rows. The rest of the skin, on the back of the neck within the region described, and that extending downward to about the eighth dorsal vertebra, was literally covered with the pointed papules described, except that in this location they were a little more deeply colored, and there were comparatively more comedo-like bodies present. The papules were evenly distributed and there was no tendency to grouping. There was no attempt at patch formation. The skin felt rough and imparted to the hand passed over it the sensation of a very fine, but stiff, brush. The papules were very close to each other, so that, from a little distance, the skin looked nearly uniformly red and, with the numerous black dots scattered all over the surface, presented a striking appearance. A few small areas of vitiligo were seen in this region.

Over the mastoids and behind and above both ears, the skin was covered with typical papules and patches of lichen planus. The same condition was seen on the posterior portion of both cheeks and temporal regions, extending to the hair line. On the rest of the face, there was a number of diffuse, erythematous patches which were raised above the surface of the skin and were covered with fine scales. They appeared to be involuting patches of lichen planus.

On the front of the neck and chest, down to about the middle of the sternum, there was a large number of acuminate papules. They were as numerous in this location as on the back, and presented the same appearance, except that there was a smaller number of black dots. The same acuminate papules were present in greater or smaller numbers on the right arm to the elbow. Below that, there were a few lichen planus patches scattered among

a larger number of discrete, acuminate papules. A few small depigmented areas were also seen in this region. On the back of the forearm, there were two large annular patches of lichen planus, enclosing within the ring formed depigmented areas like the ones on the back of the neck, only the depigmentation, was more complete. The areas were whiter and had fewer horny spines. The depigmented areas were not atrophic; the skin was perfectly normal, and except for the spines, feels smooth and pliable. The rest of the forearm had many scattered acuminate papules.

On the left shoulder and arm, there were many acuminate papules and scattered among them were lichen planus papules and patches. From the elbow to the wrist, the planus patches were larger, more numerous, of various shapes and sizes, and frequently joined each other, giving the lesion a reticulated appearance. On the back of the forearm, there was one large depigmented patch, in size about 2½ by 5 inches (6.3 by 12.6 cm.). The annular patch of lichen planus surrounding this lesion was not complete, and only segments of it were present. The portions of the vitiligo patch that had no border were adjacent to a nearly normal skin sparsely dotted with red acuminate papules. Had we divided this patch into three portions, an upper, a lower, and a posterior, the skin of the upper one would have been found a little rough. There were several enlarged follicles or papules with black props on the apex of each. In the lower segment, the skin appeared soft and smooth without any horny plugs or comedo-like bodies, with only a few pits representing dilated follicles. The skin of the posterior portion, however, was perfectly smooth and shiny, and slightly atrophic.

On the inner surface of both cheeks, there were a number of white, hard and shiny, raised papules, also lines running radially backward.

On the greater part of the rest of the body, there was a mild follicular keratosis.

There were no lesions on the posterior surface of the phalanges, the palms, or the soles.

Treatment.—The patient was given Asiatic pills (arsenous oxid and black pepper), one-fortieth grain each, with the instruction to take one three times a day and to increase the dose one pill daily until three pills three times a day were being taken. Locally, 5 per cent. rectified oil of birch tar and 5 per cent. salicylic acid in Lassar's paste was prescribed. A biopsy was made, and the section was taken from one of the patches on the left forearm, including part of the vitiligo patch, the border, and a little portion of the skin outside of the lesion.

Pathologic Findings.—The stratum corneum was thickened and was made up of superimposed wavy lamellae with spaces between them. No nuclei could be found. The stratum lucidum was not to be seen. The stratum granulosum was well developed. It consisted of a double layer of cells with coarse granules. The stratum malpighii was diminished in thickness, especially in the region near the dilated follicles. Some of the cells of the rete, especially those of the lower layers, were swollen, edematous and vacuolated. The cell was round, the protoplasm did not strain readily, and the nucleus was shriveled, pushed to one side, and occasionally compressed against the cell wall. In several instances, the walls of two adjacent cells had broken through, forming a vesicle with two nuclei. The rete pegs were diminished in size and in places had entirely disappeared. Pigment cells were entirely absent in the epithelium.

The papillae were flattened, and toward the center of the lesion they had entirely disappeared. In that location, the epidermal-cutaneous junction had

become a straight line. The upper layer of the cutis was sclerotic in places; the fibrous tissue appeared homogeneous and stained deeply with eosin. There was a diffuse cell infiltration in this layer. Often, a space containing cellular infiltrate was present between the cutis and the epithelium. A few cells of the infiltrate made their way between the cells of the epidermis, obliterating the line of demarcation between the latter structure and the corium. In the middle layer of the cutis, the infiltration was more pronounced and was mostly confined to large, well circumscribed spaces following the course of the blood vessels. The lower layer of the cutis and the subcutis were normal.

The infiltrate was made up largely of small lymphocytes, and young spindle-shaped and branched fibroblasts. There were very few polymorphonuclear cells, a small number of plasma cells, and a comparatively large number of mast cells in every portion of the field.

The hair follicle was tremendously dilated and filled with a horny plug which extended down from the horny layer of the epidermis on the surface, and reached the bottom of the follicle. A very fine lanugo hair was usually, but not always, found in the horny mass of the follicle. Occasionally the hair had fallen out and a vacant space could be seen in its place. The plug was composed of longitudinal concentric lamellae. The stratum granulosum of the follicle was thicker, and the granules were coarser, and in places had run together to form droplets. There was a marked infiltration in the fibrous sheath of the follicle which extended far out into the surrounding corium. A number of cells of the infiltrate found their way between the cells of the outer layers of the follicle, partly obliterating the latter structure. No sebaceous glands could be seen in the field. They were entirely concealed from view by the infiltrate. There was no infiltration about the sweat gland. The duct remained normal and there was no infiltration about it along its entire course through the corium. Two ducts had been traced into the epithelium. They remained normal until they had nearly reached the latter structure. There they became dilated, their walls increased to three and four layers in thickness, and the dilated mouth of each contained a small horny plug.

Most of the vessels were dilated. Occasionally a vessel was encountered in which the lumen was narrowed almost to occlusion. There was thickening of the intima, which was caused by an increase in the size and in the number of layers of its cells. The adventitia was thickened and sclerosed. The fibrous sheath was infiltrated in all vessels.

The elastic tissue appeared to be normal in the two lower layers of the cutis, except that, toward the center of the lesion, some of the fibers appeared to be thicker. In the uppermost stratum, and in the location named above, the fibers were very fine and few in number, and many of them stained blue with acid orcein-polychrome methylene blue.

August 19, there were no changes, except that most of the planus lesions were covered with fine silvery scales.

September 3, the scales on the lichen planus lesions and on the borders of the depigmented patches were very fine and furfuraceous. The lesions themselves were a little paler. The color of the acuminate papules had changed from a deep red to a light pink. There seemed to be a smaller number of black dots than formerly. The horny plugs were gray, and imparted this color to the general appearance of the skin. The latter felt rough and almost file-like. The disappearance of the color from the acuminate papules within the vitiligo patches, made the latter look paler and brought out the depigmentation more prominently.

September 6, the flat, infiltrated lesions had thinned down considerably. They were much paler, but the color was still deeply violaceous. Scaliness was present on only a few patches, while most of them had a smooth and shiny surface which was thrown into folds. On the neck, the borders of the vitiligo patches had assumed a distinct brown color. The color of the acuminate papule was that of the normal skin. With the disappearance of the color from the papules on the back of the chest, a number of them were seen to be about twice the size of the average acuminate papule. They were round, flattened, and paler than the surrounding skin. Their surface was very shiny and that made them easily distinguishable from the surrounding acuminate papules. The plugs had fallen out, and in their places was seen a minute central depression. Side by side with the lesions described, there were several minute, polygonal, shiny areas which were a little depressed below the surface of the skin and possessed no horny plugs or central depressions.

September 13, the luster of the shiny papule described before had disappeared. The color was pale, the surface dull, and the papule so distinctly different from the surrounding ones that it could be picked out at a distance. Small, irregular patches of vitiligo were seen on the back in the region of the sixth dorsal vertebra, corresponding in location to the group of shiny, depressed, and irregular little areas seen before. They differed from their former appearance in having completely lost their luster and in having run together to form small irregular patches of vitiligo without any border around them. The horny plugs had now fallen out of a large number of papules on the back of the chest. The follicles had remained dilated, and comparatively large areas of skin had assumed the appearance of coarse-grained leather. The white, radial lines in the mouth had nearly disappeared and only a few white shiny papules remained.

September 19, new patches of vitiligo had developed on the back from the already described flattened acuminate papules. New shiny depressed areas were seen on the skin over the left shoulder blade.

September 28, the annular lesions surrounding the vitiligo patches, as well as the rest of the lichen planus lesions, had nearly disappeared. In their place, there was now a deep brown pigmentation. The spines, for the most part, had fallen out and the skin was beginning to feel smooth, soft and pliable.

October 6, all old active lesions had disappeared. Depigmented patches were to be seen, surrounded by deep brown borders and scattered brown patches. Additional depigmented papules had run together to form patches.

November 19, vitiligo, pigmentation, and pitting were still present. The little props in the new depigmented areas had fallen out and the patches were white and pitted. No border surrounded these lesions. The little irregular, star-shaped and slightly depressed patches which were found in this location, and which had apparently developed in the small areas of skin between the papules, had run together to form larger patches and, in doing so, had enclosed a number of acuminate papules within the newly formed patch, so that there was no distinction between the lesions formed in this manner and those formed by the paling down and by the subsequent enlargement of the acuminate papule to the size of a small patch. Only one newly formed patch had a faint pink border around it.

December 11, the condition continued about the same. One portion of the large depigmented patch on the left forearm looked a trifle more atrophic than at the beginning. At this stage the patient left the city, and no further observation was possible.

COMMENT

At a glance it can be seen that the case closely resembled one of those described by Hallopeau. There was the same depigmented patch surrounded by a zone of lichen planus with typical lichen planus patches present on the patient. The horny plugs and comedo-like bodies were identical with those described by Hallopeau, except that in some patches they were numerous, arranged in rows, and placed in comparatively large papules. The pathologic findings agree with those of Darier, except that in the case herein described a mild infiltration, not seen by Darier, but found in Reiss' case, and in two cases of Zarubin, was present in the upper layer of the cutis. The diffuse eruption of acuminate papules situated outside of the vitiligo patches had not been seen in any of the other cases so far described. The question as to what constitutes a typical case of lichen atrophicus or sclereux has apparently not been definitely settled. In spite of the fact that all authors are practically in agreement as to the pathologic findings, there are great differences in the clinical descriptions of the cases reported. There seems to be two groups of cases. In one there is a complete absence of typical planus lesions, and the basic lesion is a white hard papule with a pink rim. The lesion in this group of cases has a closer resemblance to morphea than to any of the lichens. The other group of cases is characterized by a depigmented patch with horny plugs or dilated follicles, and surrounded by a red or violaceous border made up of lichen planus lesions. To this group belongs at least one of Hallopeau's cases, one of Zarubin's, the case reported by Reiss, and others. The vitiligo patch in Reiss' case had a sepia brown border. There is no doubt in my mind that the brown color in the last mentioned case was left after the clearing up of the annular patches of lichen planus which originally surrounded the depigmented lesions. This occurred in the case of the patient described in this article. It is quite likely that much of the disagreement in the clinical description of the lesions in the group of cases reported under the head of lichen atrophicus is due to a misunderstanding. It is probable that not all observers had the opportunity to follow up their cases long enough to be able to watch the changes in the lesions during the process of evolution and involution of the disease. For that reason, stages of the disease have been mistaken for a complete clinical picture. For the same reason, perhaps, there is also a disagreement on the question as to whether lichen atrophicus is a modification of lichen planus, or whether it is an entirely separate disease. If we subscribe to the statement of Ormsby that the papule is white from the beginning, that it is never colored, and that typical lichen planus lesions do not appear in conjunction with the depigmented lesions, we must logically assume that the disease in question is not a modification of the lichens,

but an entirely different disease. As a matter of fact, the two varieties of lesions have occurred together in a large number of the reported cases, including two of Ormsby's group. To assume that the papule is never red would necessitate the exclusion of most of the cases reported as lichen atrophicus, including some of those reported by Hallopeau, who named the disease.

The manner in which the lesion is developed has been variously described by several authors. According to Hallopeau, there are three ways in which the atrophic patch may develop: 1. A small angular violaceous papule develops a horny plug or comedo-like body in its center. That part of the papule becomes slightly pale and somewhat depressed. The papule enlarges peripherally and gradually changes into a ring with a pale center. The horny plug may fall out and leave in its place a little depression. As the lesion grows peripherally, it clears in the center. New planus papules are continually added to the border. Discrete papules are always to be found near the lesion. 2. The depigmented lesion may develop from a lichen planus patch instead of from a papule, and the result will be the same. 3. The vitiligo patch may be primary and the lichen planus border may develop secondarily around it. Csillag thinks that the primary lesion is a red conical papule. According to the observations of Crocker, the first thing to appear is a black dot: a red areola develops around it, the horny plug falls out, and the lesion becomes decolorized. Other writers describe the origin of the lesion thus: There is originally a flat or conical papule which may be round or angular or irregular in shape. According to some observers, a little scale develops on its surface, and when the scale is removed a scar-like depression remains; other papules become pale and depressed in the center without a scale being present. According to others, Ormsby included, the papule is white and hard from the start. A number of papules coalesce to form a patch. The border is not made up of lichen planus lesions, but is an extremely narrow rim of pink or red. No lichen planus papules are seen at the periphery of the lesion.

It is fortunate that the patient whose case is herewith described remained long enough under observation to throw some light on the possible mode of origin of the depigmented lesion. It was not a difficult matter to watch the stages of development of some of the lesions, as they took place in rapid succession within a short period. Unfortunately, there were no fresh lesions developing in the region in which lichen planus papules and patches were the predominating element, and therefore it is not safe to draw any conclusions as to the mode of origin of the depigmented lesions in this region, outside of what can be logically inferred, namely, that the lesions might have developed from lichen planus papules and patches in the manner

described by Hallopeau. The origin of the depigmented lesions from acuminate papules on the back of the chest, however, was plainly observed at the beginning, and was followed to the completion of the development of the patch. The lesions, formed in the small areas of skin between the red acuminate papules and inclosing the latter, suggest a mode of origin not at all unlike the one described by Crocker.

The horny plugs within the older depigmented patches can easily be imagined to correspond to the original papule and plug from which the lesion had developed, as the papules in which they are placed were small and colorless. In the younger lesions, however, the papules were comparatively large and deeply colored, and were in no respect different from those on the skin outside of the depigmented lesions. They were placed close to one another and sometimes were arranged in parallel rows. Remembering that some of the patches were in existence before the generalized eruption of acuminate papules, may we not think of the possibility that at least some of these papules made their appearance on top of previously existing patches of vitiligo? This possible mode of development of the lesion is also in agreement with one of those described by Hallopeau.

CONCLUSION

It is apparent that my case is identical, clinically and microscopically, with those described by Hallopeau and others under the title of lichen atrophicus or sclereux. The mode of origin of the atrophic patch also logically points in that direction. What has not been accounted for is the generalized eruption of acuminate papules situated outside of the depigmented patches. In spite of the fact that the papules were smaller and the plugs were more filiform than in typical cases of lichen acuminatus, these points of difference are insignificant compared with the many points of similarity of that eruption with the disease mentioned above. It is only necessary to mention the microscopic findings, the extreme itchiness, and the deep red color of the papule for a period of more than a year after the onset of the disease, and the rapid progress of the patient toward recovery after arsenic treatment, to establish the identity of the case in question with lichen acuminatus. On the other hand, the age of the patient, the occurrence of the eruption in conjunction with typical lichen planus lesions, and its appearance on the chest, which, according to Crocker, never occurs in lichen spinulosus, are strong points against its having any relation to the latter disease, the only one with which it might possibly be confused.

From what has been said, I feel justified in my belief that the case presented is one of a very rare combination of the two types of lichen, both being of the atrophic form: hence the justification of the name.

909 Kelly Street.

Abstracts from Current Literature

THE EXPERIMENTAL PRODUCTION OF SARCOMA OF THE LIVER OF RATS. F. D. Bullock and M. R. Curtis, Proc. New York Path. Soc. **20**:149 (Oct.-Dec.) 1920.

The authors in their experiments have successfully produced sarcoma of the liver in rats. They took a number of rats from five different strains, whose estimated ages varied from 2 to 9 months. They fed these rats tenia eggs from *Tenia crassicolis* of the cat. The larvae were soon found in the capillaries of the liver. Shortly after this they gradually developed a cyst wall which enclosed the parasite. From the walls of these cysts the sarcomas developed. These sarcomas were either single or multiple localized nodules in the cyst wall, which either encroached on the cyst cavity or projected externally. The tumors, they found, belonged to two histologic types, or a mixture of these, being composed of either spindle or polymorphous cells, or containing both kinds in varying proportions.

These sarcomas grew very rapidly in some cases. They sometimes replaced a large part of the liver substance and attained a size several times as great as that of the normal organ. They varied in consistency from firm and elastic to soft and brainlike, and contained many blood vessels.

Gross metastases were usually always associated with the larger tumors and frequently occurred with tumors of smaller size. Some of the secondary tumors were often the result of implantation of tumor cells, but some were true metastases. Some of the induced tumors were transplanted into subcutaneous tissues of rats and showed a high percentage of successful inoculations, thus proving their malignancy.

The tumor-bearing rats all presented multiple cysts in the liver, in number from six to eighty-four. In a high percentage of these animals only one of the cysts per animal was primarily involved in the malignant process. The tumor cyst contained larvae, the condition of which apparently depended on the state of preservation of the cyst wall, and when the cyst wall was uninvolved by the tumor, the parasite was alive; but when the cyst wall was involved in the tumor necrosis, the larva was usually dead.

The authors thought it probable that the live worm initiates the malignant process and that the death of the worm is secondary to the growth and necrosis of the tumor. The length of time for the irritation to produce these tumors varies within wide limits. A small but definite sarcoma was found as early as 248 days after the animal was fed cat feces.

The authors produced these malignant sarcomas in the livers of eighty-five rats though the mediation of *Cysticercus fasciolaris,* the larval stage of *Tenia crassicolis* of the cat. The malignancy of these tumors is based on their invasive growth, their ability to form metastases, and their transplantability to other rats.

In a discussion in which Dr. Ewing took part and brought out the point that "the rat's fibroblasts or epithelial cells or blood vessels respond to certain standard irritants much more actively than human tissues do, and if that is the case, then the significance of this sarcoma in the rat, while it is a true sarcoma for the rat, may not have so direct a bearing on the study of sarcoma

in man." Dr. Wood agrees that "a sarcoma in the rat is not a sarcoma in the human being." He stated that "it is a particular type of tumor, and it is well known that rats are apt to have sarcomata and mice carcinomata. These are biological features showing how each animal has its own peculiar tumors. The tumors were characteristic of sarcomata."

McCAFFERTY, New York.

STUDIES IN ASYMPTOMATIC NEUROSYPHILIS. I. A TENTATIVE CLASSIFICATION OF EARLY ASYMPTOMATIC NEUROSYPHILIS. ALBERT KEIDEL and JOSEPH EARLE MOORE, Arch. Neurol. & Psychiat. **6**:286 (Sept.) 1921.

Although we are as yet ignorant of the exact route followed by *Spirochaeta pallida* in its invasion of the central nervous system, we know definitely that in many cases this invasion occurs with the generalization of the infection preceding secondary manifestations. In other words, the onset of neurosyphilis coincides in most instances with the onset of syphilis. Apparently the only exceptions are those instances in which central nervous system invasion takes place during subsequent periods of generalization of the infection, such as are believed to precede recurrent outbreaks of a secondary type or by direct extension from an intimately associated focus of syphilitic bone or vascular disease. We may conclude that in untreated or inadequately treated cases more than one invasion of the central nervous system may occur. By means of routine lumbar puncture it is possible in primary and early secondary syphilis to differentiate four groups of cases: one in which the fluid is normal; a second group with minimal fluid abnormalities, such as slight increase in the globulin content and cell count; a third group in which minimal abnormalities are associated with a positive Wassermann reaction when large amounts of fluid are used and with a syphilitic zone gold curve or mastic 3 reaction, and a fourth group with maximal positive findings in all tests. In the first group fall the cases which presumably escape central nervous system invasion. In the second group, an undetermined number are probably normal, the globulin and cell increase being irritation phenomena. The third group contains principally cases of early meningovascular neurosyphilis with possibly a small proportion of cases with incipient parenchymatous or central involvement. All cases falling in the fourth group with all tests positive are obviously neurosyphilitic.

OLIVER, Chicago.

CLINICAL LECTURES ON DERMATOLOGY. LICHEN. P. G. UNNA, Dermat. Wchnschr. **72**:450 (June 4) 1921.

Lichen affects the epidermis in a manner similar to eczema and psoriasis. It is a form of inflammation of the epidermis which passes through a series of peculiar histologic and clinical standards, to attain an entirely distinctive destination. The inflammatory process attracts a stream of nourishment from the blood vessels so that the epidermis is over nourished. There is a marked hyperkeratosis, which is primary—not secondary as in callous eczema.

There is no doubt that lichen is caused by a still unknown infectious microorganism which possesses a strong power of chemical reduction. This favors an unusual cornification of the epithelium and imparts a peculiar tightness and dryness to the horny layer. The dryness is so marked that there is no parakeratosis nor accumulation of scales. The surface of the lichen papule is smooth, hard and scaleless.

The prickle cell layer also hypertrophies and shows acanthosis. There is an atrophy of the germinal layer. The picture of the prickle cell layer changes from an initial acanthosis to a later true hypertrophy without hyperplasia through the loss of the germinal layer and horizontal stratification of the now simply hypertrophic prickle cells.

In the derma similar characteristic changes occur. There is a dense small cell infiltration sharply limited to the upper cutis. In this region, in proximity to the atrophic germinal layer of the epidermis, are dense accumulations of very small cells which appear to be naked nuclei. There is marked distention of the papillary bodies.

ANDREWS, New York.

DERMATITIS AND ALLIED REACTIONS FOLLOWING THE ARSENICAL TREATMENT OF SYPHILIS. J. E. MOORE and A. KEIDEL, Arch. Int. Med. **27**:716 (June) 1921.

An interesting and complete review is given of the arsenical dermatoses occurring in twenty-three cases following the use of the arsenical products. According to the authors' report they found three times as many cases in white people as in negroes, but the presence of syphilitic lesions or duration of the disease seemed to have no effect in modifying the dermatitis. In their cases the reactions occurred early in the course of treatment and could not be attributed to either mercury or potassium iodid and the dermal lesions consisted of the usual types—macular, maculopapular, exfoliative, urticarial, erythematous, herpetic—as well as stomatitis and itching. They found that the simple erythematous types and urticaria were not serious, and in most cases did not terminate arsenical treatment, but the more severe types were accompanied by blood changes consisting of leukopenia, decrease in polymorphonuclear neutrophils, eosinophilia and increase of the transitional cells. Their patients showed a sensitiveness persisting for long periods which could always be elicited by small doses of the drug. The prognosis of the severe reactions is grave, as five of their patients died. They also found that itching without lesions but with stomatitis due to arsenic was accompanied by a blood picture similar to that found in the group of exfoliative dermatitis. They are of the opinion that the origin of the reactions of this group lies in anaphylaxis.

JAMIESON, Detroit.

LOCALIZED MALIGNANT DISEASES OF THE MOUTH AND THEIR TREATMENT THROUGH COMBINED METHODS. G. E. PFAHLER, Dermat. Wchnschr. **72**:182 (March 5) 1921.

Edged teeth, ulcerative pyorrhea, syphilis and smoking are of prophylactic importance. Ulcers, fissures, crusts and warty growths on the underlip or in the corners of the mouth, if they remain longer than three weeks, should be thoroughly treated. A positive Wassermann reaction does not warrant simple treatment by antisyphilitic remedies for months without improvement.

Combined surgical removal, local destruction by electrothermic coagulation, filtered roentgen rays and the application of radium, gain the most favorable results.

Electrothermal coagulation implies dissolution of cell structure through electric heat generated within the cell by its resistance to the electrical stream passing through it. D'Arsonval or Oudin currents of 1,000 up to 2,000 ma. and bipolar electrodes, variously constructed according to local requirements, are employed. Circumvention of the diseased area and its removal with curved

scissors after thorough electrocoagulation is the practice. In this manner all bleeding is prevented and the lymphatic channels are not opened. Supplementary treatment with filtered roentgen rays or radium over the site of the lesion and neighboring lymph nodes is usually advisable.

The severe pain caused by these treatments is best allayed by morphin or scopolamin. In some cases, ether also must be used, but the quantity of slime and hyperemia it causes and the danger of explosion make it objectionable.

ANDREWS, New York.

TROPICAL INGUINAL GRANULOMA IN THE EASTERN UNITED STATES. A. RANDALL, J. C. SMALL and W. P. BELK, J. Urol. **6**:539 (June) 1921.

It was possible for the writers to gather fifteen cases together to make this report, and they believe that this condition has been present in many cases in the temperate zone, masquerading as syphilis and various other diseases.

Pathologically, section from four cases showed a moderate proliferation of fibrous tissue, an enormous number of polymorphonuclear leukocytes and endothelial cells, chronic inflammatory thickening of the vessel walls and proliferation of the squamous epithelial cells of the skin, which in one case was so marked and extended so deeply that a preliminary diagnosis of epithelioma was made.

Direct smears were made and stained with Wright's stain, the organisms appearing as small, rounded pink bodies with a dark blue coccoid body in the center, or as oval pink bodies with a bacillary, or diplococcoid body in the longitudinal axis. Other bacteria are few in number in the smears.

The organisms were also grown on various cultures, and from their study this is shown to be a nonmotile, nonsporulent, encapsulated bacillus, gram-negative, showing metachromatic granules as well as capsules with Romanowski staining.

Their treatment consisted of tartar emetic intravenously beginning with 0.04 gm. (¾ grain) and advancing rapidly to 0.1 gm. (1½ grains), giving treatments daily for about ten days, then according to symptoms.

Rapid healing results, and eight of their eleven personal cases were cured.

JAMIESON, Detroit.

GRANULOMA INGUINALE (GRANULOMA VENEREUM; GRANULOMA OF PUDENDA; ULCERATIVE VULVITIS; SERPIGINOUS ULCERATION OF GENITALS, ETC.). K. M. LYNCH, J. A. M. A. **77**:925 (Sept. 17) 1921.

In the experience of Lynch, cases of this type have been a fairly common occurrence, though until recently, their true nature was not understood.

Two types of cases have been encountered: (1) a pure type, and (2) a type which appears to be secondary or associated with other conditions. Three cases of the first type, and six cases of the second are reported. The latter were preceded by or complicated with syphilis, gonorrhea or chancroids. One of the patients, in addition to lesions on or around the genitals, had an ulcer of the cheek. Donovan's bodies were found in all cases. In addition, Lynch records the finding of this organism in a granuloma of the back, and in three chronic ulcers of the leg.

The organism was easily obtained in smears and by culture. It was found pathogenic for rabbits when injected subcutaneously, but no infection occurred from implantation of the organism on surface abrasions.

In the pure cases, Lynch had excellent results from tartar emetic therapy; but when the condition existed as a complication of some persisting disease, as in the case of syphilis, tartar emetic alone appeared to be powerless.

MICHAEL, Houston, Texas.

LOCALIZED MALIGNANT DISEASES OF THE MOUTH AND THEIR TREATMENT THROUGH COMBINED METHODS (Con.). G. E. PFAHLER, Dermat. Wchnschr. **72**:195 (March 12) 1921.

Many areas are irradiated so that the entire periphery and the lymphatic drainage are included. The course of treatments is repeated after two weeks, and again after three weeks or a longer time. If irradiation has not preceded electrothermal coagulation it should be applied within the following day or two. The best possible result is obtained through carefully measured erythema doses corresponding to 10 X of unfiltered roentgen rays using the Kienboeck scale, producing Tint B with Sabouraud-Noire pastilles, and conforming to 10 units on a Holzknecht radiometer, filtered through 6 mm. of aluminum, or 2 mm. of glass and 4 mm. of aluminum, or delivered from a tube measuring Grade 9 Benoist, very deeply penetrating roentgen rays, so that the dose can be increased up to 30 X or three times Tint B, measured under the filter. Radium has no advantages over roentgen rays except the ease of application within cavities to cross-fire with roentgen rays.

The author discusses in detail the selection of suitable cases for the various methods, and concludes that the cases forming the report, except those involving the underlip, are almost entirely inoperable, and that every improved method of treatment is a distinct advance. Every lesion in the mouth which does not show a tendency to heal within a few weeks should be suspected of malignancy and be destroyed. Recent lesions can be treated by electrothermal coagulation with better results and with less loss of substance than by any other method.

ANDREWS, New York.

THE ICEBOX MODIFICATION OF THE WASSERMANN TEST IN THE DIAGNOSIS AND TREATMENT OF SYPHILIS. ALBERT KEIDEL and JOSEPH EARLE MOORE, Johns Hopkins Hosp. Bull. **32**:296 (Sept.) 1921.

The writers have examined a parallel series of 300 cases comparing the results of icebox to water-bath incubation. The same "set ups" were employed in performing the tests of the two methods. Plain and cholesterinized antigens were employed in the two series.

In their series of cases there were 107 presumably nonsyphilitic, 19 grouped as doubtful syphilitic, 148 treated syphilitic and 28 untreated syphilitic patients. Of the purely syphilitic cases, they found the icebox method 50 per cent. more sensitive, and, furthermore, the most striking difference was seen in the greater persistence of positive reactions by this method in treated cases. The plain extract of the icebox method produced complete fixation more frequently than the cholesterinized antigen of the water-bath.

They conclude from their results on treated cases with the icebox method that our present standards for the treatment of syphilis are probably too low. They believe that in the future the proper therapeutic control must include

repeated Wassermann reactions by the icebox as well as by the water-bath method. Further study by the authors will probably indicate roughly to what extent our present period of active treatment should be lengthened.

McCafferty, New York.

CLINICAL OBSERVATIONS ON THE MICROSPORON EPIDEMIC NOW PREVALENT IN BERLIN. A. Buschke and G. Klemm, Dermat. Wchnschr. **72**:453 (June 4) 1921.

Since the spring of 1918, a microsporon epidemic has prevailed in Berlin. The authors observed 300 cases in children from 2 to 14 years of age. Most cases occurred either as single, sharply circumscribed, well-defined plaques or as diffusely scattered multiple small patches over the entire head. Six showed kerion formation. The identity of the microsporon was established through cultures on Sabouraud's medium.

The authors state that in the beginning they used only roentgen-rays, but because of the injuries entailed by this method, they later reserved their use for recurrences which did not yield to other remedies. The ill effects of roentgen rays are enumerated as vomiting, fainting, headache, dermatitis and permanent partial alopecia. Resort was had to various antiparasitic remedies, including chrysarobin and pyrogallol. The latter was used in 5 to 20 per cent. ointments, with dynamic local reactions.

Andrews, New York.

A CONTRIBUTION TO THE QUESTION OF POSITIVE RESULTS OF THE WASSERMANN REACTION IN SOFT CHANCRE AND PUSTULAR PROCESSES ABOUT THE GENITALIA. Georg Birnbaum, Dermat. Ztschr. **33**:292, 1921.

Paradoxical positive Wassermann reactions in most nonsyphilitic diseases, scarlet fever, leprosy, malaria and typhus, are easily recognized because of the clinical characters of the disease. In soft chancre, this is not true. If a Wassermann is reported positive in clinical soft chancre, one must rule out early syphilis by spirochete investigations of the lesion or from the gland. Late syphilis may require lumbar puncture findings.

In 2,426 cases, which included 1,811 cases of soft chancre, and 615 cases of ulcerations about the genitalia, there were thirty-five doubtful or positive Wassermann reactions, twenty-eight in cases of soft chancre and seven in cases of ulcerations. The positive or doubtful Wassermann reaction must not be taken to indicate syphilis when it is the only symptom. It should be verified by repeated tests, Wassermann, Sachs-Georgi, spirochete examinations and clinical study.

Goodman, New York.

CLINICAL LECTURES ON DERMATOLOGY. ECZEMA PAPULATUM AND VERRUCOSUM. ACANTHOSIS. P. G. Unna, Dermat. Wchnschr. **72**:353 (May 7) 1921.

A slight degree of acanthosis accompanies all true eczemas. If this is elevated sufficiently to be macroscopically visible and palpable, the condition is an eczema papulatum. The term papulovesicular eczema is misleading as it applies only to the small group due to physical and traumatic irritation described by Willan, distinguishing these from the erythematous and scaly eczemas of Rayer.

Among the true eczemas there is one which is heavily acanthotic and truly an eczema papulatum. The thickening of the epidermis is not follicular. In one type there is a dry marginal acanthosis in the form of a ring, called by Hebra eczema marginatum. This may be due to fungi. If the acanthosis is greater and the elevation is from 2 to 3 mm. (1/12 to 1/8 inch) above the skin level the surface becomes warty or verrucous—eczema verrucosum. Eczema papulatum is frequently confused with pityriasiform and seborrheic eczema, and may go over into flat intertriginous eczema.

The clinical pictures of papular, marginated and verrucous eczema, except for the more or less marked elevation, are distinguished by the very different construction of the covering horny layer and its color.

ANDREWS, New York.

THE ADVANTAGE OF SERUM THERAPY AS SHOWN BY A COMPARISON OF VARIOUS METHODS OF TREATMENT OF ANTHRAX. J. C. REGAN, Am. J. M. Sc. **162**:406 (Sept.) 1921.

Regan reviews the literature dealing with the various methods of treatment of anthrax up to the present time, emphasizing their disadvantages and even dangers in some methods, such as scarring, pain, danger of secondary infection and possibility of making the local condition worse.

These older methods have no specific effect on the disease, and he advises most strongly the use of anti-anthrax serum as a local therapy, leaving the pustule to its own evolution. Surgery may be employed to supplement this treatment if necessary.

He states that the action of this serum is almost specific, and that the mortality will be reduced to a minimum by prompt recognition and early serum therapy which should be used both as a local and as a general measure. He believes that this fulfils all the requirements for an ideal treatment as it can be used at any time and in all forms of the disease, is a specific, prevents generalization if used in time and eliminates scarring and pain almost entirely.

JAMIESON, Detroit.

GENERALIZED EFFECTS OF ROENTGEN RAYS. G. STUMPKE, Dermat. Wchnschr. **73**:745 (July 16) 1921.

Local roentgen-ray reactions range from a first degree erythema to a roentgen-ray carcinoma, whereas generalized effects, which occur especially after intensive irradiation over long periods of time, are principally anemia, weakness and cachexia. The latter play a more important rôle than we are often inclined to assign to them, because our attention is constantly given to the avoidance of local reaction. In the treatment of epitheliomas it must be kept in mind that small doses stimulate the lymphocytes and that large doses destroy the blood elements.

Generalized reactions occur frequently without any local reactions preceding them, and in those with intact or undiseased skin, and usually in persistent dermatoses, such as psoriasis and eczema. Two cases of psoriasis are described which were irradiated over long periods of time. In one debility and anemia ensued, whereas in the other the number of leukocytes dropped to 2,000. Headache, syncope, general discomfort, insomnia, palpitation and similar disturbances may precede the more severe generalized reactions.

ANDREWS, New York.

PSEUDO-RUBELLA. T. S. Westcott, Am. J. M. Sc. **162**:367 (Sept.) 1921.

Attention is directed to a sporadic exanthematous disease which occurs in infants from 8 months to 2 years of age, but which is stated to be noncontagious.

The abrupt onset is accompanied by fever which rises to 103 and 104 F. by the third or fourth day, and also by enlarged postcervical glands. At the end of the fourth day the eruption begins to appear as a few discrete, pale, reddish macules, pinhead in size, about the neck, face and ears and above the clavicles. Within a few hours it has spread to the chest, shoulders and downward over the body, showing coalescence at times on the face, thighs and loins.

The lesions remain macular and much more discrete than those of rubella; the color is pale pinkish to violaceous. The palms and soles are usually spared. The rash begins to disappear by the next day and is not followed by desquamation.

The writer believes that this disease is distinct from rubella and constitutes a hitherto undescribed mild noncontagious exanthematous disease of infants.

Jamieson, Detroit.

THE CLINICAL DIAGNOSIS OF HEREDOSYPHILIS. H. F. Stoll, J. A. M. A. **77**:919 (Sept. 17) 1921.

The clinical features of heredosyphilis are discussed in some detail, especially the significance of the stigmas of the disease.

The common impression that the deciduous teeth are not affected in hereditary syphilis is not subscribed to by the author; in fact, malformations of these teeth may give a direct clue to the disease. Of the permanent teeth, hypoplasia of the sixth year molar is more common, and just as significant as are notched incisors.

Besides the more common osseous stigmas, Stoll calls attention to two less known ones. The first is an increase in the carrying angle giving rise to what he terms "knock-knee elbows" and the second is bilateral limitation of extension of the elbows.

Study of a case of suspected heredosyphilis should include a thorough investigation of the family history of the patient. This is especially important in late heredosyphilis in which the Wassermann reaction is often negative.

Michael, Houston, Texas.

CLINICAL LECTURES ON DERMATOLOGY. CALLOUS AND PRURIGINOUS ECZEMA. P. G. Unna, Dermat. Wchnschr. **72**:393 (May 14) 1921.

Marked hyperkeratosis is not one of the fundamental characteristics of eczema. It is not in the same category as parakeratosis, acanthosis, and spongiosis. The latter are moist processes, whereas hyperkeratosis signifies a drying up process, due to newly superimposed conditions which are independent of eczema. Local callosities are caused by pressure, heat and continued irritation. The same effect is produced by continual scratching. Callous eczema is the combination of the ordinary circumscribed eczema with circumscribed hyperkeratosis.

Besides scratching as a cause for callous eczema, we have in rare cases an internal cause, a constitutional anomaly of the skin, giving it a special

tendency toward hyperkeratosis. This keratophilia causes a rough, dry skin with diminished elasticity. These changes are recognized principally in the face which has a mask-like appearance. The upper eyelids are drooped, producing a characteristic tired expression.

Pruriginous eczema is a universal eczema superimposed on an inherited or acquired keratophilia. At its height there is a similarity to the prurigo gravis of Hebra.

ANDREWS, New York.

LUMBAR PUNCTURE EXPERIENCES IN THE DIAGNOSIS OF SYPHILIS. H. FUHS and G. SCHALLINGER, Dermat. Ztschr. **33**:303, 1921.

The authors report their findings in 252 cases of lumbar puncture, which included 179 untreated persons suffering from syphilis. The patients submitted to puncture in the sitting posture. The normal cell count limit was placed at four. The colloidal gold reaction was the most constant positive finding. The interesting contribution was that they sought to avoid the after-effects of puncture. A solid needle had been used to find out whether, even without fluid loss, there would be after-effects. Intravenous introduction of fluid, 500 or 1,000 c.c. (17 or 34 fluidounces) was also tried, but only repeated injections of the larger amount seemed at all useful. Pilocarpin and atropin were both tried. Injections of the choroid plexus are still in the experimental stage.

GOODMAN, New York.

PATHOLOGIC CHANGES IN SKIN DISEASES. E. PULAY, Dermat. Wchnschr. **72**:465 (June 11) 1921.

Changes in the skin are frequently expressions of derangements of the internal organs, as evidenced by an extensive literature. In recent years changes in the blood chemistry have attracted attention. The author reports a series of dermatoses examined from this point of view. Chemical analyses were made of the residual nitrogen, uric acid, calcium, cholesterin, chlorid and glucose.

In urticaria, blood analysis in three cases showed an increase of the uric acid and cholesterin and in one case an excessive increase in the calcium content and the calcium ion concentration. The augmentation of these substances causes an anisotony which irritates the sensory nerves, causing itching, and the sympathetic nerves, causing hyperemic, cutaneous manifestations.

Ordinarily pruritus is a sensory neurosis. In a universal form it frequently accompanies icterus, diabetes, chronic diseases of the kidneys, stomach and intestines and the rheumatic diathesis. Examination of six cases showed an increase of urea in the blood, and in one case there was hyperglycemia, while in two cases the calcium content was diminished. A vagotonia was recognized in all cases, possibly dependent on diminished calcium content, or osmotic disturbances due to the increased blood urea. The vagotonia quickly yielded to the administration of atropin.

ANDREWS, New York.

PATHOGENIC CONSIDERATIONS ON GENERAL PARALYSIS. L. MARCHAND, Presse méd. **70**:697 (Aug.) 1921.

The author discusses the syphilitic nature of general paralysis based on two points: first, spirochetes have been found in cases of general paralysis; and, second, the Bordet-Wassermann reaction is always positive in the spinal

fluid. The author confines himself in the greater part of the article to the views of other well-known writers in regard to the inefficiency of treatment in paresis, the strain of spirochetes in paresis, its location and the damage done.

The writer advances the view that the spirochete is not solely responsible for general paralysis, but depends on a secondary organism, probably a filtrable virus, which causes the changes so frequently seen both clinically and pathologically. He believes that the spirochete probably prepares the way. He supports his theory on the ground that the spirochete is hard to isolate; the uncertainty of the Wassermann reaction and its positive reaction in the spinal fluid in other conditions; the localization of the spirochete in the nervous parenchyma away from the meningeal and vascular lesions; the inefficiency of treatment, and, lastly, the presence of paresis in persons who deny syphilitic infection and in whom no clinical evidence can be found of a syphilitic nature.

McCafferty, New York.

SILVER ARSPHENAMIN AND SULPHOXYLATE. THEIR COMBINATION IN THE TREATMENT OF SYPHILIS. T. Katz, Dermat. Wchnschr. **72**:554 (July 2) 1921.

The usefulness of mercury in the treatment of syphilis has diminished in recent years. The malnutrition of patients as a result of the war has made them more susceptible to the poisonous effects of mercury on protoplasm. Numerous cases of nephritis and stomatitis have limited its value.

Silver arsphenamin alone is employed in early syphilis. It affects lesions not only as well as the old treatment with combined mercury and arsphenamin but has an equally favorable influence on the Wassermann reaction. However, it has no lasting effects.

Sulphoxylate is a good supplementary remedy. Its results are permanent. The combined silver arsphenamin-sulphoxylate treatment of syphilis is supplanting the treatment with mercury and obtaining early cures with less bodily injury.

Andrews, New York.

ACTION OF RADIUM AND ROENTGEN RAYS ON NORMAL AND DISEASED LYMPHOID TISSUE. I. Levin, J. A. M. A. **77**:930 (Sept. 17) 1921.

Levin and his associates have ascertained in a series of clinical and experimental investigations that the lymphocytes circulating in the blood are most readily influenced by radium and roentgen rays, while all the other normal types of leukocytes and the erythrocytes possess a greater resistance.

Normal lymphoid tissue is less radiosensitive than the various types of hyperplasias of lymphoid tissue. Simple inflammatory hyperplasias are less sensitive than the neoplastic hyperplasias.

Roentgen rays and radium have not only an effect on the lymphoid elements of the part irradiated, but local irradiation appears to influence all lymphoid structures. It is impossible to assert at present what the mechanism of this influence is.

Cure of a case of status thymicolymphaticus is recorded by radium and roentgen-ray treatment. Similar treatment resulted in marked benefit in cases of Hodgkin's disease, mediastinal tumor, lymphosarcoma, lymphatic leukemia and myeloid leukemia.

Michael, Houston, Texas.

SOME OBSERVATIONS ON THE USE OF ARSPHENAMIN: ITS EFFECT ON THE KIDNEYS AND ITS THERAPEUTIC RESULTS. H. B. ANDERSON, Am. J. M. Sc. **162**:80 (July) 1921.

Thirty-nine patients with syphilis were selected for study who had each received twenty or more doses of arsphenamin over at least a two year period. Functional kidney tests failed to show any conclusive evidence of kidney injury. The writer believes that in diagnosis at least two antigens should be used, preferring the acetone insoluble antigen as the safest guide in diagnosis, but the cholesterinized alcoholic extract in determining treatment. He also states that the average patient with secondary or tertiary syphilis will require at least twelve or more doses of arsphenamin accompanied by a corresponding amount of mercury to produce a negative Wassermann reaction, which will probably become positive without further treatment.

JAMIESON, Detroit.

THE PROPHYLACTIC USE OF TRYPAFLAVIN IN VESICULAR ERUPTIONS OF THE SKIN. E. ARNING, Dermat. Wchnschr. **72**:359 (May 7) 1921.

Trypanosomal diseases were early shown to have special susceptibility to acridin dyestuffs and particularly to a yellow dyestuff, the diaminomethylacridinium chlorid, which received the name trypaflavin. Soon the value of this group of remedies was excelled by the intensive action of the atoxyl group and the discovery of arsphenamin.

Through the work of Browning and Kolle a new field for the chemotherapeutic use of the acridin dyestuffs and particularly trypaflavin, as the remedy with slightest toxicity for the body and greatest toxicity for pyogenic microorganisms, was created.

The author believes that the normal impenetrability of the horny layer to pyogenic organisms is lost in vesicular eruptions, and that much of the toxicity of certain diseases, such as pemphigus, bullous erysipelas and dermatitis herpetiformis, is due to the penetration of pyogenic micro-organisms through the impaired epidermis. He has painted the lesions of pemphigus with trypaflavin with good results. A 2 per cent. solution in equal parts of alcohol and water was employed. Large doses were injected intravenously with benefit. No deleterious renal effects were noted.

ANDREWS, New York.

PATHOLOGIC CHANGES IN SKIN DISEASES. E. PULAY, Dermat. Wchnschr. **72**:511 (June 25) 1921.

Chemical examination of the blood of five patients with psoriasis revealed a normal uric acid content in all cases. The author avers that this discounts the theory of purin retention. In each instance there was an increase of residual nitrogen, cholesterin and chlorid content. One case presented a hyperglycemia. These changes suggested a retention of renal origin. The theory is advanced that there is a capillary sclerosis of the blood vessels of the skin analogous to that observed in the kidney in diffuse glomerulonephritis.

Fourteen cases of seborrhea were examined for changes in blood chemistry. There was an increase of residual nitrogen, chlorid and cholesterin in every specimen studied. In four cases of acne rosacea and one of angioneurotic edema, similar disturbances were noted.

ANDREWS, New York.

SULPHOXYLATE ARSPHENAMIN. Leo Kumer, Dermat. Ztschr. **33**:322, 1922.

This preparation has not yet been placed on the commercial market. It differs from all others of the arsphenamin group in being a fluid, and in being sealed into ampules as a fluid. The drug is easily prepared by diluting and injecting, without anything further being done. The drug is thought to be about on a par with neo-arsphenamin, but not as potent as silver arsphenamin, from the experiments on recurrent fever and rabbit syphilis. The maximum dose is given as 0.3 gm. (4½ grains), with intervals of from six to eight days between doses, and no more than 2 or 3 gm. (31 or 46 grains) are given in any course because of fear of cumulative effects.

The human cases did not altogether confirm the animal experiments. Spirochetes were still seen and actively movable 115 hours after the first, and 45 hours after the second injection, whereas 96 hours had been the experimental limit. The clinical results were fair. The serologic changes were promising. By-effects as from other arsphenamins were noted.

Goodman, New York.

INTERNAL HYDROCEPHALUS IN A SYPHILITIC, PROBABLY DUE TO INTRASPINAL TEATMENT. A Keidel and J. E. Moore, Am. J. Med. Sc. **162**:209, (Aug.) 1921. R

This is a report of an interesting case, illustrating the possibilities of intracephalic disturbance following intraspinal therapy. Pain followed the first intraspinal treatment and persisted for several days. Later severe occipital headaches returned which did not improve under continued treatment. After intervals of rest and treatment, the patient improved somewhat, but eighteen months after the first treatment symptoms of intracranial pressure were noted, and on puncture the spinal fluid spurted out a distance of several inches. A decompression operation was performed about three months later, with subsequent great improvement. Six months after operation, the patient reported that his condition was practically unchanged and that he was partially incapacitated by headaches.

The authors have come to the conclusion that the first intraspinal treatment set up a severe aseptic meningitis which produced a mass of adhesions about the subarachnoid space, thus causing a partial occlusion of one or more of the three foramina of exit. Disappearance of the adhesions or the formation of a new foramen of exit is stated to be the only chance for a recovery.

Jamieson, Detroit.

A NEW METHOD FOR STAINING SPOROTRICHUM BEURMANII IN TISSUES. G. Pacinotti, Riforma med. **37**:733 (July) 1921.

The author advises the following technic for staining the fungus in the tissues: the sections, made as thin as possible with the freezing microtome, are washed in distilled water and then treated with diluted alcohol and pure alcohol for one hour. The sections are then stained with gentian violet or methyl violet for three or four hours at room temperature, washed several times in absolute alcohol in order to remove the excess of stain, and then treated with absolute alcohol in which a few crystals of picric acid have been dissolved. The fungus appears deeply stained by the violet and the surroundings are greenish-yellow.

Pardo-Castello, Havana.

PATHOLOGIC CHANGES IN SKIN DISEASES. E. PULAY, Dermat. Wchnschr. **72**:489 (June 18) 1921.

In accord with Brocq, the author considers eczema the principal manifestation of an exudative diathesis, analogous to arthritism, hay fever, asthma, gout and migraine. Seven cases were examined as to blood chemistry. All showed an increased calcium content and an increased calcium ion concentration in the blood. The uric acid content was raised. In three cases a hyperglycemia existed. Itching, edema, vesiculation, exudation and erythema are clinical manifestations of disturbed hydroxyl-ion concentration and electrolytic equilibrium.

Investigation of two cases of prurigo demonstrated a high blood uric acid, suggesting the physicochemical etiology of the pruritus similar to that observed in urticaria.

ANDREWS, New York.

NOTE ON THE PRESERVATION OF STOCK STRAINS OF TREPONEMA PALLIDUM AND ON THE DEMONSTRATION OF INFECTION IN RABBITS. W. H. BROWN and L. PEARCE, J. Exper. M. **34**:185 (Aug.) 1921.

Experiments have shown that rabbits inoculated with old strains of *Spirochaeta pallida* cannot terminate the infection although developing a resistance to the toxic effects. The lymph nodes have been found to harbor the organism indefinitely, and it is proposed to inoculate a sufficient number of rabbits with different strains so that the pallidum could be recovered at any time by the excision of a lymph node and inoculation of the testes. If it is desired to obtain any particular organism, the inoculation should be made about six or eight weeks before needed.

JAMIESON, Detroit.

THE SPECIFICITY OF THE PRECIPITATION REACTION OF SACHS-GEORGI AND MEINICKE. W. GAEHTGENS, Dermat. Wchnschr. **73**:724 (July 9) 1921.

After an examination of seventy-two patients with the Wassermann, Sachs-Georgi and Meinicke reactions, the author concludes that the precipitation reactions of Sachs-Georgi and Meinicke are distinguished by a great specificity for syphilis. Rarely nonspecific results occur with tuberculous serum. Occasional failures should not prejudice the practical significance of these methods, because all biologic reactions, including the Wassermann test, have their limitations. In these instances frequently weak reactions come into question, which on second control investigation often do not recur. As greater delicacy is attained by extending the time of observation in the Sachs-Georgi reaction to forty-eight hours before evaluating the precipitation for serologic diagnosis, this modification is recommended.

ANDREWS, New York.

EXPERIMENTAL SYPHILIS IN THE RABBIT. VII. AFFECTIONS OF THE EYES. W. H. BROWN and L. PEARCE, J. Exper. M. **34**:167 (Aug.) 1921.

The affections of the eye which might follow infection (testicular) include conjunctivitis, ciliary injection, keratitis or iritis, either singly or in combination. There was found to be a common focus of infection in the episcleral tissues from which point it spread to the conjunctiva and cornea or

to the ciliary body iris and choroid. In most cases the eye lesions were only generalized lesions or were the last lesions to appear, and relapses were very frequent. It is believed that these tissues have little protection induced by reactions elsewhere, and it was found possible to increase or diminish the severity of these lesions by experimental means.

JAMIESON, Detroit.

LICHEN VARIEGATUS? E. G. GRAHAM LITTLE and SIR WILLIAM WILLCOX, Proc. Roy. Soc. **14**:92 (Sept.) 1921.

The patient, a woman, aged 24, had an eruption which had been ascribed to exposure to chemical substances in a munition factory in which she had worked two years before. After leaving the factory she developed a yellow color, and a part of the rash followed. The unusual feature was the curious lichenoid follicular eruption on the back, and especially on the thighs. There was an appearance of a remarkable degree of striae cutis distensae. The presenters did not think the munition work had anything to do with the appearance of the eruption, but were not prepared to say what the eruption was. It was not of long duration, not more than two years, and she was getting well.

GUY, Pittsburgh.

THE TOXIN TREATMENT OF DERMATITIS VENENATA. A. STRICKLER, J. A. M. A. **77**:910 (Sept. 17) 1921.

Strickler reports further experiences with extracts obtained from various poisonous plants, such as poison ivy. Suitably diluted, the appropriate extract is injected intramuscularly every twenty-four hours. Usually only two injections are needed, but sometimes three or four have to be given.

Thirty patients have been treated in this manner without a failure. The pertinent facts of seventeen cases are recorded. As a rule, the subjective symptoms disappeared or were greatly ameliorated within twenty-four hours after the first injection. The experiences of Alderson and of Petch, equally favorable, are likewise noted.

Strickler believes that this method of treatment has a curative influence on rhus dermatitis, and that, in practically all instances, desensitization is accomplished by it. At present, it is not possible to say how long an immunity acquired in this way will last, but it is probably temporary in nature and must be renewed from time to time.

MICHAEL, Houston, Texas.

THE ABORTIVE AND GENERAL TREATMENT OF SYPHILIS. W. RICHTER, Dermat. Wchnschr. **72**:437 (May 28) 1921.

Statistics concerning the results of the abortive treatment of syphilis are at such variance that syphilis, before the appearance of the secondary stage, is subdivided into the preprimary, seronegative primary, and seropositive primary stages. The first consists of a minute erosion, after a suspicious intercourse, in which spirochetes can be found. As abortive treatment, injections of arsphenamin are given every five days until eight doses have been administered. Locally glacial acetic acid was used as a caustic. In later stages of syphilis similar courses of arsphenamin were accompanied by injections of soluble mercury every other day, aggregating twenty doses.

ANDREWS, New York.

URTICARIA, CLASSIFICATION OF TYPES AND ITS CAUSES. G. L. LAMBRIGHT, Am. J. Med. Sc. **162**:183 (Aug.) 1921.

Lambright thinks the following classification according to etiology is of assistance: The cases nonsensitive to proteins are divided into (1) neuropathic, (2) chemical and (3) constitutional. Cases sensitive to proteins are divided into seasonal and non-seasonal, of which the former may be due to (1) pollens, (2) bacteria, (3) foods, (4) animal proteins; the non-seasonal may be due to (1) foods, (2) bacteria, (3) animal proteins.

He uses the usual cutaneous reaction to determine the specificity of food sensitization and cites instances in which the various factors have been the exciting cause of the urticaria.

JAMIESON, Detroit.

ERYTHEMA FIGURATUM PERSTANS. H. W. BARBER, Proc. Roy. Soc. **14**:89 (Sept.) 1921.

A woman, aged 38, presented an eruption which consisted of ringed erythematous patches, first appearing sixteen years before around the right axilla. A few years later, similar patches appeared near the groins and the lower abdomen, and during the last two years behind the knees. As a child she had had repeated attacks of tonsillitis, with quinsy, and her tonsils were scarred and septic.

The case corresponded to the one which was originally reported by Dr. Colcott Fox in the "International Atlas of Rare Skin Diseases," under the title of "Erythema Gyratum Perstans," and similar cases have been described by Wende and Mook.

GUY, Pittsburgh.

TARTAR EMETIC FOR VENEREAL GRANULOMA. W. E. GIBLIN, Brit. M. J. **1**, June 18, 1921.

The author reports eighty-four cases of venereal granuloma treated with intravenous injections of tartar emetic. In every instance the patient left the hospital apparently cured after a course of this treatment. This method was used: A 1 per cent. tartar emetic solution is filtered and boiled for two minutes. The injection, given on the same day, is 10 c.c. containing 0.1 gm. (1½ grains) and is given intravenously twice weekly for ten injections. An interval of ten days is allowed to elapse and then five more injections are given. In men the dose can be increased up to 0.15 gm. (2⅖ grains) but no higher. The beneficial effects are apparent after two injections.

OLIVER, Chicago.

COMPARATIVE RESEARCHES BETWEEN THE REACTIONS OF SACHS-GEORGI, MEINICKE AND WASSERMANN. E. ARNING, Dermat. Wchnschr. **72**:400 (May 14) 1921.

Of 916 specimens of serum studied according to the technic of Meinicke and that of Wassermann, 9 per cent. gave dissimilar reactions. The Sachs-Georgi reaction was applied to 1,025 specimens and gave a result similar to the Wassermann reaction in 88 per cent. The author concludes that the Sachs-Georgi reaction is not as specific for syphilis as that of Meinicke, and that both methods for the time being should be considered only as supplementary to the Wassermann reaction.

ANDREWS, New York.

A CASE OF DERMATITIS DYSMENORRHEICA SYMMETRICA. L. BAER, Dermat. Wchnschr. **72**:535 (July 2) 1921.

The patient was a 19-year old girl who had suffered from menstrual disorders since puberty. She was congenitally feebleminded, and had hypoplastic genitals. Subsequent to each menstrual period for the past year there had appeared red macules on the cheeks associated with generalized itching and burning. In the course of a few days these became either vesicles or nodules, or secondarily infected from scratching. The case was carefully observed to exclude factitious dermatitis. Brauer ascribes these cutaneous disorders to the actions of hysterical persons, whereas Polland accepts the menses as the directly etiologic factor.

ANDREWS, New York.

PHENOLS IN THE URINE IN PELLAGRA. M. X. SULLIVAN and P. R. DAWSON, Arch. Int. Med. **28**:166 (Aug.) 1921.

It was found that the phenol excretion of the pellagrins studied showed little variation from the normal either in amount of total phenols or in percentage of conjugation. Most of their cases were of a mild type and only three out of sixteen showed an increase in the active stage. With increased protein metabolism, the authors think there is also increase in the phenols. Indican gave a marked reaction in ten out of twelve cases.

JAMIESON, Detroit.

CONTRIBUTION TO THE TREATMENT OF SYPHILIS BY INTRAVENOUS MERCURY. FRIEDRICH WEISE, Dermat. Ztschr. **33**:328, 1921.

Mercury injected intravenously has given no indication either clinically or serologically of being a potent drug in syphilis. Several preparations were tried. These included afridol (63 per cent. of mercury) and enusol (38.6 per cent. of mercury and 14.4 per cent. of arsenic). Symptoms of intolerance were encountered even when the preparations were given in autoserum. Spirochetes could be demonstrated in the lesions in one case even after large doses had been administered. These unfavorable results are about the same as those reported from the Jena clinic.

GOODMAN, New York.

ARSPHENAMIN DERMATITIS. J. TROEBS, Dermat. Wchnschr. **72**:550 (July 2) 1921.

The author has observed seven cases of arsphenamin dermatitis within the last two years, during which period 2,000 injections have been given. The cause of the eruption in two patients was neo-arsphenamin; in three, silver arsphenamin and in two, neo-silver arsphenamin. The dermatitis following the administration of the last mentioned preparation was in each instance very severe. In spite of this fact, neo-silver arsphenamin is advocated as an excellent remedy to which the most serious syphilitic symptoms respond promptly, and by which the blood reaction is always favorably influenced.

Fixed exanthems are regarded as angioneurotic syndromes due to incomplete solution of the powder. When dilute silver arsphenamin solutions are used these fleeting exanthems apparently do not occur.

ANDREWS, New York.

THE ETIOLOGY OF IMPETIGENOUS PARONYCHIA (TOURNIOLE-SABOURAUD) AND PEMPHIGUS NEONATORUM. E. DELBANCO, Dermat. Wchnschr. **72**:362 (May 7) 1921.

The author describes a case of pemphigus neonatorum in which the patient died in the exfoliative stage. Simultaneously with the death of the child, the mother developed a blister on the tip of the right index finger. Microscopic examination of the contents of the lesion revealed numerous staphylococci. Histologic study of the dead infant's skin did not reveal definite staphylococci, or many pus cells. However, the author suggests a possible identity of the two diseases.

ANDREWS, New York.

ATROPHIC CONDITION OF SKIN FOLLOWING TREATMENT OF NAEVUS. E. G. GRAHAM LITTLE, Proc. Roy. Soc. **14**:89 (Sept.) 1921.

At the time of presentation a woman, aged 29, had a patch of dead white atrophic skin spreading from the summit of the shoulder, the site of the original scar from a nevus treated with acid, across the left breast, in an area the size and shape, roughly, of the palm of a man's hand. There did not seem to be any perceptible sclerodermic tissue but the diagnosis of scleroderma was considered. There seemed to have been no redness nor ulcerative condition.

GUY, Pittsburgh.

THE TREATMENT OF TUBERCULOUS ADENITIS BY ROENTGEN RAYS AND RADIUM. R. H. BOGGS, Am. J. M. Sc. **162**:90 (July) 1921.

Radiation is recommended as the method of choice in the treatment of tuberculous adenitis as it leaves no scar, produces atrophy and destruction of lymphatic foci and suppurating glands and is not followed by recurrences. Ninety per cent. of cases treated by this method are reported to be cured without surgical measures of any sort, although surgery may be employed for the removal of hard fibrous nodules that sometimes remain, but which contain no tuberculous foci. Other cervical glandular enlargements are also amenable to radiation, but not always with such success as that which follows treatment of the tuberculous type.

JAMIESON, Detroit.

ABSENCE OF THE UPPER LATERAL INCISORS AND CONGENITAL SYPHILIS. W. GAERTNER, Dermat. Wchnschr. **72**:505 (June 25) 1921.

Absence of one or both upper lateral incisors is a common occurrence. The absence may be inherited, or the tooth may be retained in the alveolar process unerupted, or may be the result of extraction. Noneruption is frequently an indication of a slight displacement of the germinal layer increasing the distance to the mucous membrane, so that the tooth, although fully developed does not pierce this structure.

Following examinations of the teeth of 2,600 children, the author concludes that syphilis is merely one of the many causes of the absence of the upper lateral incisors and a relatively rare inconsequential factor.

ANDREWS, New York.

POLARISCOPIC STUDY OF URINES OF A GROUP OF SYPHILITICS. S. P. TAYLOR and K. P. A. TAYLOR, Am. J. M. Sc. **162**:47 (July) 1921.

In this work the urines of fifty syphilic patients were studied to determine whether the presence of albumin and casts in a large percentage might indicate a specific nephropathy. Seventy-two per cent. of these cases showed varying degrees of albumin without any clinical evidence of nephritis, 44 per cent. had albumin and casts and 56 per cent. an excess of epithelial cells, most of the latter having received intense treatment with arsphenamin. None of the urines studies showed the double refractile lipoids.

JAMIESON, Detroit.

TABES DORSALIS IN THE EARLY STAGES OF SYPHILIS. H. FUHS, Dermat. Wchnschr. **73**:721 (July 9) 1921.

The combination of tabes and early syphilis is rare. Four cases are reported by the author. In all there were secondary papular eruptions involving the genitals, anus and tonsils. The spinal fluid in two patients showed a pleocytosis and in all cases the diagnosis of incipient tabes was confirmed by serology or neurologic examination.

According to Fournier, secondary syphilids occur not infrequently in the very late stages of syphilis, but thorough investigation warrants the belief that the author's cases do not fall into this rôle.

Involvement of the central nervous system in the early stages of the disease responds with unusual readiness to mercury-sulphoxylate treatment.

ANDREWS, New York.

LYMPHOPENIA FOLLOWING EXPOSURES OF RATS TO "SOFT" X-RAYS AND THE BETA RAYS OF RADIUM. J. C. MOTTRAM and S. RUSS, J. Exper. M. **34**:271 (Sept.) 1921.

It was found that after a dose of soft roentgen rays administered to rats there was a diminution of lymphocytes on an average of 58 per cent. one hour after irradiation. The size of the dose is referred to as a "twelve" dose, using the equivalent of a ¾-inch point-to-point spark gap. A corresponding exposure of radium was followed by a decrease of 38 per cent., this being attributed to a lower penetrating power of the beta rays compared to the "soft" roentgen rays.

JAMIESON, Detroit.

SYPHILIS AND MARRIAGE. A. JORDAN, Dermat. Wchnschr. **72**:543 (July 2) 1921.

The course of syphilis at present is milder than it was before the era of arsphenamin, and cases free from residues are more frequent than formerly. In cases in which the disease is acquired through marriage it is shown that in an overwhelming majority the husband is responsible for the infection. The author believes that marriage is permissible in patients who have been under mercury and arsphenamin therapy for three years, are residue-free and have negative Wassermann reactions.

ANDREWS, New York.

SOME URINARY CHANGES IN NORMAL INDIVIDUALS ON THE PELLAGRA PRODUCING DIET. M. X. SULLIVAN, Arch. Int. Med. **28**:119 (July) 1921.

Six normal persons were placed for five days on a pellagra producing diet such as was used at the Rankin farm.

Marked urinary changes were produced, as there was a decrease in volume, as well as in total and urea nitrogen. The ratio of urea nitrogen to the total was markedly lowered, while the ammonia was increased. After four days on the diet the urinary findings were similar to those of active pellagrins.

JAMIESON, Detroit.

A CASE OF ACNITIS BARTHELEMY. W. VOIGT, Dermat. Wchnschr. **72**: 529 (July 2) 1921.

A case of acnitis is described, the eruption occurring in a young tuberculous subject. Shotty nodules, hard and movable, appeared on the nose and cheeks, later on the ears and temples. The skin over them was bluish red, without scaling. In a few there was cell formation with central necrosis. The eruption further spread to the sides of the neck, the sternal region, the penis and the backs of the hands. Histologically there were tubercles about the blood vessels. Under tuberculin therapy the manifestations completely disappeared.

ANDREWS, New York.

THE TREATMENT OF CUTANEOUS ANTHRAX. W. H. OGILVIE and A. W. HALL, Brit. M. J. **2**, June 18, 1921.

In a short but interesting article published in answer to an article previously published in the same journal concerning the treatment of this disease with serum alone, the writers attempt to show that in a series of cases at Guy's Hospital, London, the combination of excision and serum treatment is probably the most rational and safest course in all cases of cutaneous anthrax which have not reached the stage of septicemia.

OLIVER, Chicago.

HYPERKERATOSIS BLENORRHAGICA. F. CARMINOW DOBLE, Proc. Roy. Soc. **14**:91 (Sept.) 1921.

A man, aged 29, who had had arthritis as a complication of gonorrhea was presented with a well marked hyperkeratosis of both soles, with several patches like broken blisters about the ankles. Blood serum, vaccines and neo-arsphenamin were mentioned as treatment.

GUY, Pittsburgh.

THE ABORTIVE TREATMENT OF SYPHILIS. R. WAGNER, Dermat. Wchnschr. **72**:433 (May 28) 1921.

Of fifty cases of early chancres with negative serology, twenty-six cases were observed for fifteen months. All patients were treated with small doses of neo-arsphenamin and silver arsphenamin. Twenty had no relapse. The results did not justify the recommendation of small doses of arsphenamin given in courses for early chancres, but served as an interesting experiment for the study of the biologic changes caused by the virus.

ANDREWS, New York.

A CONTRIBUTION TO THE HISTOLOGY OF LICHEN SIMPLEX CHRONICUS, VIDAL. ARTHUR ALEXANDER, Dermat. Ztschr. **33**:251, 1921.

Alexander studied sections from eleven cases of lichen simplex chronicus. He is led to believe that there are only three differences, histologically, between lichen chronicus and eczema. Lichen chronicus does not have a stage of phlyctenization or true vesicle formation. There is no depigmentation of the basal epithelial layer. There is a tendency to emigration of leukocytic cells from the papillary and subpapillary layers.

Alexander would not admit that the two diseases are the same on clinical grounds alone, even if histologic technic should not demonstrate a single anatomic difference.

GOODMAN, New York.

CONTRIBUTIONS TO THE BIOLOGY OF SPIROCHAETA PALLIDA. W. BRUCK, Dermat. Wchnschr. **72**:641 (July 2) 1921.

In the examination of three early nonulcerated chancres with Meirowsky's osmium-panchrome method and with Hermann's fixative, the author discovered numerous forms of spirochetes comparable to those described by Meirowsky. There were many knotted forms, some pedunculated, and some with club-shaped swellings, and lateral branchings. A number of Japanese authors have confirmed these findings. Noguchi has described a great number of round, refractive granules in the periplasm of spirochetes. These changes are more likely a phase in the life cycle of the organism than a result of plasmolysis.

ANDREWS, New York.

CONTRIBUTION TO THE QUESTION OF IDIOSYNCRASY TO X-RAY. P. HESS, Dermat. Ztschr. **33**:333, 1921.

Hess takes the stand that idiosyncrasy to the roentgen ray has not been proved. He cites a case of a patient who received an unfiltered dose of roentgen ray which was intended for filtered administration. If the act of forgetfulness had not been noted, this case could have been taken as an example of idiosyncrasy. Such lapses in technic may be more frequent than admitted.

GOODMAN, New York.

ABORTIVE TREATMENT OF SYPHILIS. E. DELBANCO, Dermat. Wchnschr. **72**:440 (May 28) 1921.

In reply to Leven and Meirowsky (*Dermat. Wchnschr.*, 1921, No. 4), who state that syphilis should be considered as a disease lasting decades, showing continuous changes in clinical and serologic symptoms, the author favors the acceptance of a single stage for syphilis, although this conception is revolutionary. A negative Wassermann reaction does not give the slightest justification for considering the body free from spirochetes.

ANDREWS, New York.

REPORT OF TWO CASES OF BLASTOMYCOSIS. W. B. HOWES and P. F. MORSE, Boston M. & S. J. **185**:315 (Sept. 15) 1921.

This article contains case reports of two cases of cutaneous and pulmonary blastomycosis.

LANE, Boston.

A CASE OF KERATOMA PALMARE ET PLANTARE HEREDITARIUM WITH INNUMERABLE STREPTOCOCCI IN THE STREAK-LIKE VACUOLIZED HORNY LAYER AND DISTURBANCES OF SENSATION. H. Nass, Dermat. Ztschr. **33**:338, 1921.

A case report with the noteworthy features mentioned in the descriptive title.

Goodman, New York.

KERATODERMA BLENORRHAGICA. E. G. Graham Little, Proc. Roy. Soc. **14**:90 (Sept.) 1921.

A man, aged 45, with a history of gonorrheal rheumatism twenty years before, was presented, with a horny medallion-like growth on the dorsal surface of the feet, accompanied by a marked cachexia.

Guy, Pittsburgh.

UNRECOGNIZED SYPHILIS. Malcolm Seymour, Boston M. & S. J. **185**:288 (Sept. 8) 1921.

This article contains an appeal for the physician to consider syphilis as a possible diagnosis more frequently, with a statistical summary of its prevalence and case histories of four patients referred because of general medical symptoms.

Lane, Boston.

Society Transactions

SILESIAN DERMATOLOGICAL SOCIETY

Breslau, June 29, 1921

CAMPHOR OIL TUMORS. Dr. Bothe.

A woman had developed camphor oil tumors in the last five or six years; twenty-four years ago she had received injections of camphor oil. Diagnosis must differentiate this condition from syphilis and tuberculosis.

SUMMER PRURIGO. Dr. Braendle.

A girl, aged 13, has for the past seven years developed pustular and vesicular eruptions every spring. There is no cicatrization. Roentgen-ray treatment has been helpful.

ULCERS OF THE GENITALS. Dr. Schneemann.

Dr. Schneemann reported two cases of deep ulceration on the genitals. Gonococci, spirochetes and Ducrey bacilli were not found. Only paradiphtheria bacilli could be demonstrated in one case. Phenol-iodoform treatment effected cure, though slowly.

LUPUS ERYTHEMATODES DISCOIDES. Dr. Liebrecht.

The eruption was on a typical location on the face. The Pirquet and Moro reactions were positive. The combined quinin-iodin treatment was successful.

ERYTHEMA INDURATUM BAZIN ON LEFT LEG. Dr. Leschinski.

The skin reactions (Pirquet) were positive. While roentgen-ray treatment completely failed, a tuberculin cure proved successful.

LOCALIZED MYXEDEMATOUS ALTERATIONS OF THE SKIN. Dr. Burchard.

Histologically, diminution and decay of the elastic fibrils, with an accumulation of mucin in the cutis were found. The general symptoms pointed to an incipient myxedema.

KERATOSIS FOLLICULARIS. Dr. Siemens.

A case of keratosis follicularis contagiosa very much resembling Brooke's was found in a boy. The mother of the patient had formerly developed the same symptoms. Besides plaques in the comissures of the mouth, circumscribed verrucous keratoses of the hands and soles were predominant.

ARSPHENAMIN EXANTHEM. Dr. Schaefer.

The patient had pronounced hyperkeratosis of the palms and lower regions of the face. The mucosa of the buccal cavity was covered with a lichen ruberlike exanthem.

DERMATITIS DUE TO INSECT POWDER. Dr. Frei.

A papular and vesicular itching exanthem was developed due to an aromatic nitrobody contained in insect powder.

MUNICH DERMATOLOGICAL SOCIETY

July 7, 1921

LICHENOID SYPHILIS AND PERIOSTITIS OF THE OS FRONTALE. Dr. Thieme.

A patient, aged 29, developed painful swelling on the os frontale and a lichenoid exanthem on the trunk and limbs. While the glands were hard and swollen there was no scar on the penis. An extragenital infection was assumed.

A CASE OF PSEUDOXANTHOMA ELASTICUM. Dr. Heuck.

Histologically the elastic fibrils, particularly in the lower layers of the cutis, were deformed into thick twisted masses, while the superficial layers of the cutis showed symptoms of a slight edema.

EPIDERMOLYSIS BULLOSA HEREDITARIA IN A GIRL AGED FOUR. Dr. Kiendl.

Therapeutically autogenous serum injections were made. This disorder may be confused with impetigo contagiosa.

BERLIN DERMATOLOGICAL SOCIETY

July 12, 1921

A CASE OF PURPURA MAJOCCHI. Dr. Arndt.

There was petechia on the lower part of the limbs surrounded by pigmented skin. Histologically, inflammation of the upper skin layers and extravasation of blood were found. The etiology was unknown. Local treatment had no effect.

CHRONIC EQUINIA. Dr. Gottron.

After neo-arsphenamin and mercury had failed to cure, irradiation was successful, although the author could not decide whether the effect was entirely due to these.

OSTEITIS PAGET DEFORMANS. Dr. Arndt.

In a woman, aged 52, who had suffered from rheumatism for a year, swelling and deformation of the tibia followed. Congenital syphilis as the causative factor was assumed.

THE SELF-CURE OF SYPHILIS. Dr. Lesser.

With mercury the proportion of the spirillicidal dose is to the toxic dose 1:1. In neo-arsphenamin the proportion is 1:10. In monkeys and rabbits mercury proves spirillicidal only in doses which at the same time cause poisoning and death of the animals. Lesser demands clear distinction between an effect on the syphilitic products and the direct effect on the spirochetes.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 10, 1921

Jay Frank Schamberg, M.D., *Presiding*

HYPERKERATOSIS. Presented by Dr. Greenbaum for Dr. Schamberg.

B. B., a negro stevedore, aged 20, born in Virginia, was first seen in May, 1921, when he exhibited follicular prominences, limited to the nose and adjacent parts of the cheeks and forehead, of four months' duration. He was not seen again until September, when it was noted that the region affected had increased in area and a lichenoid condition of the neck had developed. Some follicles on the cheeks presented miliary pustules, without infiltration at the base. Sections from a biopsy showed follicular hyperkeratosis and slight granulosis. The Wassermann reaction was negative.

DISCUSSION

Dr. Knowles observed that it was certainly a curious location for such an eruption but that, after noting the marked keratosis pilaris which existed on the extensor surfaces of the patient's forearms, it would seem possible that the facial outbreak was a part of that disease.

Dr. Schamberg said that the patient undoubtedly had keratosis pilaris on the arms but he had never seen the disease on the face. The nose, chin and cheeks were covered with distinct follicular prominences. Microscopically, there was distinct keratosis. He felt it should be classed as an unusual keratosis follicularis. Possibly, it was an incipient case and later manifestations would make this more evident.

Dr. Hirschler asked the patient concerning drug administration preceding the eruption, but a negative history was forthcoming.

Dr. Schamberg added that there was pigmentation and roughening on the neck, shoulder and upper arm. No spiny plugs were in evidence.

Dr. Strauss called attention to the occasional pustules in the follicular orifices. The regions affected were more deeply pigmented, especially the face, which was very black, much darker than other parts of the negro's skin.

ERYTHEMA MULTIFORME. Presented by Dr. Warren Walker.

E. D., a ship carpenter, aged 23, white, unmarried, had had six attacks of erythema multiforme. They had all occurred in the months of May and October. The last outbreaks had been preceded, by two days, by extensive herpes of the lower lip. The type of lesion had been bullous throughout, and the situations of the erythema multiforme had been uniformly on the backs

of the hands and neck. The case was presented on account of the curious relationship between the herpes labialis and the erythema.

CICATRICES FOLLOWING BURNS. Presented by Dr. Knowles.

J. D., a Jewish dealer, aged 60, had been severely burned by ignition of a barrel of alcohol. His hands and forearms were terribly scarred, and his fingers were being drawn in various directions by cicatricial contractures. He was presented for suggestions for treatment.

DISCUSSION

Dr. Weidman mentioned the occasional reports of the use of a pepsin-hydrochloric acid mixture in the treatment of cicatrices and keloids.

Dr. Schamberg touched on one treatment which proved of value in the war but which required special appliances: ionization. Other than that he could offer as suggestions only surgery and manipulations.

Dr. Strauss reported good results in some patients with the pepsin-hydrochloric acid treatment but said that in others it had proved too irritating. This remedy was also said to have been used hypodermically.

CASE FOR DIAGNOSIS. Presented by Dr. Strauss for Dr. Knowles.

H. S., a colored housewife, aged 33, had previously been in good health. Six children were living and healthy. One miscarriage occurred three years ago. The present condition began in July, 1921, as a few scattered papules and nodules situated mainly on the arms and legs, although a few occurred on the trunk and neck. The lesions were firm and tended to flatten out gradually. There was no itching complained of. On a placebo treatment, some of the lesions were partially absorbed. The Wassermann reaction was negative. The differential blood count showed: polymorphonuclears, 54 per cent.; eosinophils, 2 per cent.; small mononuclears, 37 per cent.; large mononuclears, 5 per cent.; transitionals, 2 per cent. A biopsy had been taken, but sections had not yet been studied.

DISCUSSION

Dr. Weidman thought that the diagnosis lay between a corymbiform syphilid, a sarcoid and miliary lupoid.

Dr. Knowles said that sarcoid was especially considered when the case was seen at the Jefferson Dispensary.

Dr. Schamberg said that it appeared to be sarcoid, but he would not attempt a positive diagnosis without examination of sections of the tissue removed. He stated that sometimes sarcoid lesions underwent spontaneous involution.

PEMPHIGUS WITH CICATRICIAL TENDENCY? Presented by Dr. Greenbaum for Dr. Schamberg.

J. V., a white schoolboy, aged 6, developed an eruption in June, 1921. At that time, small blisters were said to have appeared on the neck. When first seen by the speaker in August, 1921, there were blebs in the cervical, axillary and inguinal regions, as well as on the forearms and legs. When presented, the patient exhibited few unbroken blebs, but many areas of a cicatricial nature, the sites of former lesions. While under observation, the patient passed through several eruptive outbreaks. At times lesions appeared on the mucous membrane of the mouth.

DISCUSSION

DR. SCHAMBERG remarked that the patient was vastly improved. When he saw him several weeks ago, at the height of an outbreak, there were scores of blebs present. He inquired as to the treatment received.

DR. KNOWLES pointed out considerable staining in the affected regions and called attention to the grouping present.

DR. GREENBAUM added that the patient was receiving sodium arsenate injections. Formerly he was taking solution of potassium arsenite (Fowler's solution). The pigmentations preceded the arsenic administration.

DR. SCHAMBERG said that the case resembled the type of pemphigoid dermatitis seen in children after vaccination. These cases ran a relatively benign course and were improved by arsenic. On the other hand, the bullous dermatitis of adults had a high fatality rate.

DR. KNOWLES asked what the last speaker deemed the proper course when arsenical treatment alone gave improvement in a given case and at the same time produced marked keratosis.

DR. SCHAMBERG felt that the latter was usually the lesser of two diseases.

EXPERIMENTAL MINERAL OIL TUMORS IN A MONKEY. Presented by DR. FRED. D. WEIDMAN.

This was one of two monkeys injected subcutaneously ten months ago with several oils, both with and without camphor. The details will be published later. The animal was exhibited to show the unequivocal manner in which the lesions were developed. Out of sixteen points injected, there had been seven "takes."

LINEAR EDEMA OF THIGHS IN MENSTRUATING MONKEY. Presented by DR. FRED. D. WEIDMAN.

This consisted of two symmetrical bands of *subcutaneous* edema—unaccompanied by any hyperemia—extending from the groin downward, over the front of the thighs, half-way to the knees.

The two bands began as narrow strips at the same region in the groin, but diverged and broadened as they extended downward. At intervals of an inch (2.54 cm.) or so they were transversely depressed, so that they really consisted of a linear series of lumps. They were soft, translucent, watery and of the same color as the sound skin. There was no evidence that they were itchy.

This was a not uncommon phenomenon in this animal. She did not develop them at every heat, but the presenter had seen at least three such outbreaks. It was probably a normal, physiologic process, an extension from the even more marked swelling which always occurred around the genitalia of several monkey species at this period. The genital swelling was also accompanied by a brilliant red hyperemia; and the face was also strongly reddened, but not swollen.

In relation to human dermatology, the foregoing observations were deemed noteworthy in two respects: first, on account of the aggravation of symptoms commonly complained of in acne vulgaris and rosacea; that is, is the explanation of these exacerbations a phylogenetic one? In the second place, the occurrence of cutaneous edema in an "experimentable" animal, particularly when in connection with a definite organic system, opens up a vulnerable point for research attack, as to the nature of various forms of edema, etc.

DISCUSSION

DR. KNOWLES asked what preparations of oil had been used in the injections.

DR. WEIDMAN replied that three oils, mineral, cottonseed and olive, had been employed. The mineral oil alone "took." Positive results were seldom obtained with animals.

DR. SCHAMBERG said that these growths were evidently analogies of the paraffinomas produced by injections for cosmetic reasons, and those produced in the buttocks and other parts from injections with mineral oil bases.

PEMPHIGOID ERUPTION WITH LUPUS ERYTHEMATOSUS. Presented by DR. CORSON.

J. M., a Russian, a baker, aged 48, a year ago, noted a red, scaly patch developing on the nose and adjoining areas of the cheeks. Six weeks ago, a bullous eruption appeared in groups over the sternum, in the axillae, on the neck and in the inguinal folds. One lesion was observed on the buccal mucous membrane. Some itching was complained of. The lesions had been appearing in crops and were seldom seen as tense blebs, but mainly as raw areas and wrinkled, flaccid bullae, averaging about 1 cm. (⅖ inch) in diameter. Possibly their early rupture was due to scratching, but the roof was undoubtedly thin. The raw areas persisted some time without marked crusting. The patient had been taking some internal medication, the nature of which was not ascertained, for the lupus erythematosus, but this had been stopped more than three weeks previously, and still the crops of bullae continued to appear.

DISCUSSION

DR. SCHAMBERG said the eruption on the face was unquestionably lupus erythematosus. That on the body was independent of the former condition. The future would determine whether it was a true pemphigus or a pemphigoid outbreak. He advised cultivation of the contents of an unbroken bleb for streptococci.

DR. CORSON added that on the latter hypothesis an ammoniated mercury salve had been used for over two weeks, but with no favorable result.

DERMATITIS LICHENOIDES PRURIANS OF NEISSER? Presented by DR. KLAUDER for DR. SCHAMBERG.

F. G., a native white factory worker, aged 19, exhibited an eruption which had been present since the age of 5 years. Erythematous, eczematous lesions were present on her face and forearms. At the latter site the patches were lichenoid: elsewhere the lesions consisted of small nodules, when discrete. Itching had always been intense.

DISCUSSION

DR. KNOWLES asked how the case was to be distinguished from one of lichen planus. It was frequently difficult to differentiate lichenoid eczema and lichen planus from eruptions of factitious origin. Some of the nodules above the patch on the wrist had the appearance of an induced eruption.

DR. KLAUDER replied that the character of the outbreak—nodules being present for a long time—and the fact that the eruption was also located on the face, seemed to differentiate the two. Before the roentgen ray was used there were more nodular lesions than at present. At first it was diagnosed as

lichenoid eczema, but later he thought it fitted in with Neisser's dermatitis lichenoides prurians. It had been constantly present since the age of 5.

Dr. Greenbaum said the patient had pruritus and later lesions appeared. At first he thought it was a case of pruritus with lichenification—Brocq's group—lichen simplex chronicus. At one time all disappeared under roentgen-ray therapy and later recurred.

Dr. Corson asked whether the eruption had ever assumed annular form, as there was a suggestion of such shape in places. One edge of the forearm patch was somewhat festooned.

Dr. Klauder had never noted ring lesions. As to its possible origin from factitious sources, the history of the outbreak was confirmed by the mother, which he felt was a strong point. A section showed infiltration of the derma—nothing else.

Dr. Schamberg was not familiar with dermatitis lichenoides prurians. On the wrists there was a resemblance to lichen simplex chronicus. The isolated lesions strongly resembled prurigo nodularis though trauma from scratching gave indurated and fibrous nodules.

PRURIGO NODULARIS. Presented by Dr. Fred. D. Weidman.

V. L., a white housewife, aged 48, in whom the disease began thirteen years ago, in the form of extremely itchy nodules having the distribution seen today, said that one of the nodules had not gone away for thirteen years. She presented excoriated, deep-seated nodules, sparsely scattered over the entire body, save head, face and shoulders, and ranging in size up to that of a large pea. They were more closely placed over the extensor surfaces than the flexor, and yet a few could be found on the flexure of the wrist. The younger ones were hard, of the same color as the sound skin, only elevated the skin slightly, and were recognized more by touch than by inspection. Older ones extended definitely above the surface, were hard, like old fibrous tissue, and strongly purple, and their surfaces were scaly. There were no extremely minute examples representing earliest formations; the process developed from the first within the comparatively large bulk of tissue to which it was limited. Sections were made from two nodules, one early and the other late. The early one showed masses of lymphocytes, placed on a much more delicate fibrous tissue reticulum than is normal for the corium. The foci occurred for the most part deeply in the corium, and not necessarily in the vicinity of appendages or vessels. The interpretation placed on the processs was a localized splitting of the collagen into fine strands, accompanied by hyperplasia of the "nuclei of the bundle" and the appearance of lymphocytes. In the older lesion, the changes were strongly restricted to the perivascular and periglandular lymphatics. They consisted of a very broad and dense lymphocytic infiltrate, with none of the fine reticular appearances or hyperplasia of fibroblasts.

DISCUSSION

Dr. Hirschler recognized the patient as one formerly treated by her—a common experience at our meetings—both at her office and at the Polyclinic Dispensary. She had given sodium cacodylate and considered the case one of typical prurigo nodularis.

Dr. Knowles had seen the case at the Pennsylvania Hospital and agreed in the diagnosis.

Dr. Weidman had made no blood examination. He had found no enlarged nodes. Sections were made from two nodules, one early, the other late. The older one was less satisfactory for study. Scaly lesions make poor sections.

Dr. Schamberg, after examining a section, pronounced it typical. With Dr. Hirschler, several years ago, he had reported cases like this. The hyperkeratosis was enormous, equal to the combined thickness of the derma and epidermis. The disease was not as rare as it was formerly regarded. Recently he had had three in private practice, one of them characterized by scores of lesions and violent itching. Some nodules were primary, and others secondary and due to scratching.

PSORIASIS OF PALMS AND SOLES. Presented by Dr. Sidlick.

T. N., a white boy, aged 6, had had a scaly papular eruption generalized in distribution and exhibiting marked preference for the palms and soles. The condition had been present one year. On the trunk, the lesions were typical guttate lesions of psoriasis, and the palms and soles showed sharply marginate patches covered with a thick white scale.

DISCUSSION

Dr. Klauder did not altogether agree with the diagnosis. The disease bore a resemblance, to his mind, to the acrodermatitis perstana of Hallopeau.

Dr. Schamberg said that psoriasis of these regions could not be expected to assume the characteristic appearance of the disease in other parts. In this case, there was marked predilection for the hands and feet.

Dr. Hirschler remarked on the well defined border of the lesions.

Dr. Greenbaum said that the diagnosis of pityriasis rubra pilaris suggested itself to him.

GENERALIZED LICHEN PLANUS ERUPTION PRECEDED BY A PRIMITIVE PATCH. Presented by Dr. Schamberg.

M. E., aged 24, presented an extensive eruption of lichen planus involving the entire trunk and extremities. On the left side of the abdomen was an oval pigmented patch about 4 cm. (1⅗ inches) in length by 2 cm. (⅘ inch) in width. This patch was of a brownish color and was studded with poorly formed lichen planus papules. The patient gave a clear and distinct history that this patch preceded the outbreak of the general eruption by two weeks. Adjacent to this patch were several small fingernail size patches, which also showed pigmentation.

DISCUSSION

Dr. Greenbaum had seen an article recently published in which it was suggested that lichen planus might be due to a spirochete. It had been seen to develop, however, in patients under arsphenamin treatment.

LICHEN PLANUS. Presented by Dr. Dengler.

F. F., a white man, aged 40, presented an unusually widespread eruption of lichen planus. Papules appeared three or four months ago, and gradually spread to all regions. Itching was severe. Lesions were present in the mouth and especially typical lesions existed on the backs of the hands.

DISCUSSION

DR. SCHAMBERG observed that there was a great opportunity for research with a view to discovering the cause of lichen planus.

LEPRA. Presented by DR. GREENBAUM for DR. SCHAMBERG.

F. C., a Jewish housewife, aged 50, came from Russia nineteen years ago. There had never been evidence of skin disease until six months ago. Just prior to that time, she had been told that she had diabetes mellitus. When first seen by the presenter, she exhibited a generalized eruption of pinkish nodules, some of which showed central necrosis. There was likewise a yellowish discoloration of the face, and irregular yellowish brown areas on the chest. No disturbance of temperature or pain sensations were observed. Nasal smears proved negative for acid-fast organisms, even after the administration of potassium iodid, and despite the presence of a perforated septum. The ulnar nerve was not appreciably enlarged. The Wassermann reaction was negative. The histologic findings consisted, briefly, of gram-positive, acid-fast bacilli in granulomatous tissue. The patient was being treated with chaulmoogra oil, given by mouth.

DISCUSSION

DR. SCHAMBERG commented on the curious central necrosis of the small nodules in certain regions. The entire arm was pitted with small depressions.

DR. HIRSCHLER remarked on the syphilislike translucency of many of the lesions.

ERYTHEMA INDURATUM. Presented by DR. KLAUDER.

An overnourished white girl, aged 17, a factory worker, had had ulcerations appearing at intervals over the posterior surfaces of the lower legs, since the age of 10. She exhibited a healing ulcerative area on the lower third of her left calf. Around the lesion were pigmented, somewhat depressed scars. Otherwise, the patient was in good health. The Wassermann reaction was negative.

DISCUSSION

DR. SCHAMBERG said that the general nutrition of this patient was of the type not infrequently seen in these so-called scrofulous dermatoses. Often conditions of over-weight or well-nourishment seemed to add no protection from these diseases.

DR. GREENBAUM thought the history peculiar as to the breaking down of the lesions, but Dr. Schamberg considered it by no means rare.

CYSTIC EPITHELIOMA. Presented by DR. MUNSON for DR. KNOWLES.

J. C., a white woman, aged 35, a Russian by birth, had small growths in the sulci between the alae of the nose and the adjacent cheek. For the last six years, they had slowly increased in growth. They were reddish to yellowish-brown and formed on each side a small cluster of somewhat translucent, semiglobular tumors, sessile and varying in size from that of a pinhead to that of a small pea. There were a half dozen members in each group. When a biopsy was taken, they did not collapse, although there was a resemblance to cysts. The hemorrhage was free.

DISCUSSION

DR. WEIDMAN recalled seeing the case at the American Dermatological Meeting in Philadelphia, about three years ago. The case was shown by Dr. Hartzell. At that time, the growths were punctured, but no fluid obtained. Soft granulomatous tissue seemed to be present. Some held it to be a cystic epithelioma, others a colloid degeneration.

DR. SCHAMBERG was inclined to agree that the case was one of cystic epithelioma.

LYMPHANGIOMA OF EXTERNAL CANTHUS OF EYE. Presented by DR. FRED. D. WEIDMAN.

M. C., white, aged 55, had a subjectively symptomless tumor at the external canthus of the eye for four years. It began like a "wart." On the first visit, she showed a congeries of four or five translucent cysts projecting far above the skin surface and aggregating the size of a small pea. There was no inflammation. It was regarded as a lymphangioma, excised and sectioned. The case was presented in view of the microscopic features, which at first sight might suggest hydrocystoma on account of the low cuboidal cells lining the cysts. But more careful study showed other smaller spaces which were not so round, but elongated. The cuboidal character of the lining of the larger cysts was an expression of reversionary metamorphosis or anaplasia.

DISCUSSION

DR. SCHAMBERG, after examining the slide exhibit, thought it was suggestive of hydrocystoma.

DR. WEIDMAN thought it was lymphangioma, on account of other spaces nearby, with simple flat endothelial lining.

RESULT OF ROENTGEN-RAY THERAPY IN PREMYCOTIC STAGE OF MYCOSIS FUNGOIDES. Presented by DR. KLAUDER.

A. Y., a native born American, aged 43, a clerk, had been under observation with a premycotic dermatitis for the last four and a half years. He had changed from one medical adviser to another and had been seen in former meetings here. Roentgen-ray therapy at one institution had been discontinued on account of the resultant toxic symptoms which followed each treatment. Commencing two months ago at the Polyclinic Hospital, all cutaneous lesions on the trunk had been treated twice and the lesions on the face and arms had been treated once. At each treatment there was administered one unit to the trunk and three-fourths unit to the face and arms. As a result of the foregoing procedure, itching had diminished about 75 per cent., according to the patient. Clinically, the lesions were markedly improved.

DISCUSSION

DR. STRAUSS remembered that this patient came to Jefferson Hospital in Dr. Stelwagon's time and showed at first only one patch over the sternum, which was regarded as a seborrheic dermatitis.

DR. KNOWLES said he was familiar with the case and that there was more improvement than in other similar cases he had seen.

PSORIASIS. Presented by DR. DENGLER.

J. P., an Italian laborer, aged 60, a hunchback, showed an eruption of flat scaly papules, generalized in distribution. The size was nearly uniform and guttate throughout, but the characteristics differed in various regions. On the trunk the lesions were typically psoriasiform, but on the forearms they were nearly equally divided between papules with pearly white scales and others with dark keratotic and seborrheic crusts. The eruption had all appeared a year and four months ago. It was very itchy. The patient had come under observation only that morning and no opportunity had been afforded to study the case carefully.

DISCUSSION

DR. SCHAMBERG thought the eruption was certainly of a very unusual type. Peculiar keratotic lesions were present, with some characteristic psoriatic papules.

SARCOID OF BOECK. Presented by DR. FRED. D. WEIDMAN.

The patient, A. H., was a colored housekeeper, aged 40. The disease began as nodules on the nape of the neck three years ago, and had never gone away. The nodules had not ulcerated. The disease next developed on the ear, elbow and face. The smallest lesions had been present five months. They had never been painful but had itched a little. The patient showed two types of lesions. The first of these were groups of translucent, smooth, shiny nodules at the nape of the neck, the groups up to the size of a half dollar and the individual nodules up to that of a split pea. In addition, on the extensor surface of both forearms there were about half a dozen small, flat-topped translucent nodules, with slightly depressed centers and a beaded margin, suggesting epithelioma. The second type was a purplish, diffuse, edematous-looking tumefaction, involving the whole upper half of one ear and several stretches along the rim of the other, resembling lupus edematosum. Over the forehead and upper half of the cheeks there were placques up to a centimeter (⅖ inch) in diameter, of the same translucent, purplish to ham-red color, but they were not so tumefied and edematous looking. There were three or four very small isolated ones over the upper chest, and a group of large ones over the left elbow. Of the latter, the largest was deep purple, the remainder red. The lower extremities and abdomen were clear. Section from the smallest nodules at the nape of the neck gave the classical picture of Boeck's sarcoid.

DISCUSSION

DR. SCHAMBERG regarded the lesions on the ear as part of the condition existing on the face, but evincing more of a neoplastic tendency. Some situations bear tumor formations, others bear nodules.

DR. WEIDMAN mentioned that the tendency to grouping at the back of the neck suggested dermatitis papillaris capillitii.

DR. SCHAMBERG continued that the ordinary history of the latter was an enormous lymph cell infiltration followed by a fibrous change. In the sections of the sarcoid nodule, the Langhans giant cells showed up in numbers.

DR. WEIDMAN proposed arsphenamin treatment. One or two reported cases presented tubercle bacilli. He had failed to produce tuberculosis material from one of his cases injected into a monkey.

DR. SCHAMBERG said that the organisms were possibly so few that inoculation was unsuccessful.

CASE FOR DIAGNOSIS. Presented by Dr. Sidlick for Dr. Knowles.

J. D., a French Canadian, aged 47, had a group of nodules in his scalp over the occiput, and a more superficial, irregularly annular patch on the extensor surface of the left forearm below the elbow. Both were reddish brown in color, intensely itchy, and distinctly infiltrated. The former patch had been present five years, the latter two and a half years. The Wassermann reaction, at first negative, became positive after a single arsphenamin injection. Further treatment had no effect on the eruption.

DISCUSSION

Dr. Schamberg thought the lesions were not syphilitic; therefore, naturally, they did not disappear under arsphenamin treatment. The patch in the scalp looked like pruriginous lesions, from scratching, resulting in infiltration.

Edward F. Corson, Secretary.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, Oct. 19, 1921

Arthur W. Stillians, M.D., *Presiding*

CASE FOR DIAGNOSIS. Presented by Dr. Eisenstaedt.

An Italian, who had been in America for thirty years, presented a lesion on the nose which was first noticed eight months ago, and which later involved the lips. The lesions were symmetrical. The one on the nose was a deep ulcer, heavily crusted and somewhat infiltrated. Near this lesion were two scars, one on the ala and one on the tip, and there was a similar scar on the right side of the nose. Two months ago the lesions cleared up without any therapy and then recurred. The teeth were in bad condition. The patient's wife had had one miscarriage twenty-one years ago, but six children were living and healthy.

DISCUSSION

Dr. Foerster thought the lesions were ulcerative lesions of late syphilis as the crusting and scar formation were such as are seen in that condition.

Dr. Zeisler thought it was tertiary, nodular, ulcerating syphilis.

Dr. Ormsby agreed with Dr. Foerster and Dr. Eisenstaedt.

Dr. Senear agreed, and said that he saw a patient two months ago with numerous gummas of the tongue who, while under treatment with mercury and potassium iodid, developed a gummatous ulcer on one side of the upper lip. The ulceration was similar to either one of those in this case, and it healed readily under arsphenamin treatment.

Dr. Stillians said he had thought of the early ulcerative lesions of syphilis which are often fairly symmetrical, but these were rather deep for that, and too few.

Dr. Eisenstaedt thought Dr. Senear brought out an interesting point regarding the similarity of the lesions in his case and in this one. He had

presented the patient because of the late symmetrical syphilitic lesions. In his opinion the symmetry of the lesion on the lip was unusual in such a late stage.

A CASE FOR DIAGNOSIS. Presented by Dr. Senear.

A man aged 39 years, about a year ago developed on the palm, fingers, forearm, penis and ankles bullae which had persisted for from seven to ten days. He had a second attack from three to four months later, a third three months after that and a fourth in June, 1921. The present attack had begun on the day of presentation, and the patient showed erythematous patches of various sizes in the locations mentioned.

DISCUSSION

Dr. Ormsby thought the case was an example of phenolphthalein dermatitis. He stated that he had seen similar cases in which the patient would not admit having taken any medicine, but practically all of the patients were found to have taken a laxative. This patient admitted having taken a laxative the night before the eruption appeared.

Dr. Foerster agreed that it was a dermatitis medicamentosa, but thought Dr. Wise's cases showed a marked chocolate brown discoloration which was missing in this case. However, this man had persistent erythema and probably would develop the chocolate brown discoloration later.

Dr. Eisenstaedt thought the diagnosis was correct. At first glance he had considered it a toxic erythema, but with the lesions in the palm and the history of taking a laxative, he thought nothing else could be considered.

Dr. Senear agreed with the diagnosis and in substantiation of Dr. Ormsby's remarks said he had asked the man at the time of the previous attack whether he had taken any drug, and he said he had not. Dr. Senear presumed the patient did not consider a laxative as medicine. All of the attacks were well characterized by bullae the size of a large hen's egg occurring in exactly the same place.

A CASE FOR DIAGNOSIS. Presented by Dr. H. B. Frost (by invitation).

A man, first seen six months ago, gave a history of a more or less generalized eruption which had persisted for two years. The eruption consisted of fine, papular lesions accompanied by more or less intense itching.

The family and previous history were negative. He was married and had two children living and well.

DISCUSSION

Dr. Pardee thought it was a case of dermatitis herpetiformis.

Dr. Foerster agreed with this diagnosis.

Dr. Ormsby thought it was a characteristic location for this disease, and stated that they saw more patients with lesions about the shoulders and elbows and over the sacrum than in any other areas.

Dr. Frost said the original diagnosis was psoriasis. His first diagnosis was dermatitis herpetiformis, but some had thought it a tinea.

VERRUCOUS NEVUS. Presented by Dr. Finnerud for Dr. Ormsby.

A Czecho-Slovakian, aged 18 years, presented a generalized eruption, which began ten years ago on the palmar surfaces and dorsa of the thumbs and first

metacarpals as a diffuse, warty thickening, at first without sensation but later accompanied by much itching. The eruption was limited to these areas until six months ago, since which time it had spread to the forearms, axillae, forehead, trunk and lower extremities, in about that order of appearance. The lesions occurred chiefly in lines following scratching. New lesions were still appearing.

Follicular keratoses and dermatitis were present in the areas mentioned, the latter the result of local treatment and scratching.

A biopsy of the dorsum of the left thumb showed marked hyperkeratosis and acanthosis with little involvement of the corium except for some vascular and connective tissue proliferation of the upper portion. A complete report of this case will be submitted at a later date.

DISCUSSION

DR. SENEAR considered the case interesting and unusual. The distribution and appearance of the lesions, particularly those in the crural region, resembled closely the lesions seen in that location in linear nevi, and he believed it was a nevoid condition.

DR. BAER thought a good many of the lesions looked like lichen planus, and it was a question in his mind whether it might not be a lichen planus arranged in this distribution.

DR. MCEWEN called attention to the fact that some lesions had been present for ten years and that they had become more generalized only two years ago. Such being the case, he thought it hardly probable that linear nevus was present. While the lesions were generally acuminate, some of those on the back were flat-topped and polygonal and typical of lichen planus. He offered a diagnosis of atypical lichen planus.

DR. ORMSBY thought it was a lichenoid nevus. It was not unusual for such patients to have a few lesions early in life and at 16 or 18 to have a marked extension of the process. It was rather anomalous to call such conditions nevi, but the patients constantly gave such a history. The warty lesions not infrequently continue to develop until the patient reaches the age of 18 or more. Histologically there was no sign of lichen planus in this case.

DR. PARDEE agreed with the diagnosis of nevus.

DR. EISENSTAEDT was in accord with this diagnosis.

DR. FINNERUD said that the case was presented with the diagnosis of nevus. When first seen the lesions were limited to the forearms and hands, and only within the last six months had they become extensive. Only the new lesions resembled lichen planus.

LESION ON THE TONGUE. Presented by DR. PARDEE.

A man, aged 45 years, first seen on account of a number of small keratoses on the palms, which had readily disappeared, incidentally had mentioned the condition on his tongue, and it was for this that he was presented. There was no history of syphilis, and the Wassermann reaction was negative, but he had shown some improvement under antisyphilitic therapy. There were no subjective sensations except a little smarting on eating sour food. The lesion had been present for five years and consisted of an apparently denuded area about 1 inch (2.54 cm.) in width, not round but nearly square, slightly depressed beneath the surrounding surface and bounded by deep sulci which separated

it from apparently normal tissue. It was covered with an adherent yellowish pseudo-membrane which disappeared leaving the lesion a slightly deeper red than normal. There was no induration apparent, and by palpation the lesion could hardly be detected.

DISCUSSION

DR. FOERSTER did not wish to offer a diagnosis without more careful study, but suggested the possibility of syphilis.

DR. BAER called attention to the improvement that was said to have occurred under antispecific treatment.

DR. SENEAR made no definite diagnosis, but believed a carcinoma of the tongue which had reached the point at which it would ulcerate to the extent seen would show much infiltration about it. There was no evidence of this, and Dr. Pardee said there was no infiltration. He had thought of the possibility of a carcinoma or a tuberculous lesion.

DR. PARDEE said the lesion had been present for five years and had hardly changed at all. He did not know what the condition was, but it was not a gumma and not a mucous patch, and it did not look like any syphilitic lesion he had ever seen. It was not an ulcer and had almost a membrane over it which could be removed with any mild antiseptic. He had burned it down with nitrate of silver and had tried to get the little sulci around the edge to freshen up, without success. He had given potassium iodid and mercury, but the general character of the lesion had not changed under any treatment. He had not used arsphenamin because the patient objected to this.

A CASE FOR DIAGNOSIS. Presented by DR. QUINN.

A man, aged 24 years, a janitor, presented a papular eruption on the back which had been present for the last ten years. The lesions were about the size of a dime, and there was evidence of scar formation and atrophy. He denied a history of smallpox or chickenpox, also syphilitic infection, but he had had a Neisserian infection seven years ago. He received several injections of arsphenamin from a physician in New York.

The urine was slightly alkaline, with a trace of albumin and many pus cells. The Wassermann reaction was negative.

DISCUSSION

DR. EISENSTAEDT thought it similar to the case presented by Dr. Pusey some months ago as a multiple benign tumor-like new growth of the skin. He offered this as a diagnosis.

DR. SENEAR said this was his idea of the case. Dr. Pusey's case had the typical hernia-like tumors on the chin, while those on the back were the exact prototype of these, but not so numerous.

DR. ORMSBY said this process was essentially an atrophy of the skin, because the elastic tissue was gone, and he believed "new growth" was not justified in the title.

DR. FOERSTER asked whether this was not the type of disorder Buzzi and Schweninger described.

DR. SENEAR said that Dr. Pusey made the diagnosis in his case from the article with the picture in the original "Ikonographia."

A CASE FOR DIAGNOSIS. Presented by Dr. Finnerud for Dr. Ormsby.

A Polish woman, aged 38 years, presented a lesion which occupied most of the right forearm. She first noticed it eight years before as a silver dollar-sized red, shiny patch. There was never any subjective sensation. The lesion had gradually become larger and darker blue-red. There had been no ulceration.

DISCUSSION

Dr. McEwen thought it was a primary progressive atrophy.

Dr. Baer agreed.

Dr. Senear agreed, and stated that he saw one of the cases reported by Dr. Wise several years ago and did not remember that it showed the definite isolated lesions which were present in this case.

Dr. Frost thought it was an atrophy of the skin.

Dr. Ormsby asked whether Dr. Senear classed it with the idiopathic atrophies of the skin, or with the Herxheimer group, acrodermatitis chronica atrophicans, which are preceded by infiltration.

Dr. Senear, replying to Dr. Ormsby, said he thought it was the type which is preceded by infiltration. By stretching the skin one could see atrophy of the deeper layers.

Dr. Ormsby thought it certainly had that appearance, but it might be an atrophy due to syphilis. Dr. Fordyce had shown a case of this type in which the atrophy was much like that seen in the cases preceded by infiltration, but which in his case proved to be due to syphilis. In this case there were no positive findings.

Dr. Finnerud said he did not know how far down the atrophy extended, but thought it extended well into the fatty layer, and that group of cases was placed under a separate head. One of the signs of that disorder was to try to pick up the atrophic skin which seems to be very loose and which lies in wrinkles and folds, but which it is found cannot be picked up because it is attached to fibrous tissue underneath. In his opinion the case was an example of "atrophy of the fatty layer of the skin," like that reported by Gilchrist and Ketron.

Dr. Foerster called attention to the dimpling and creasing of the skin, and that it was possible to push the skin into the deeper tissues, where it would remain, just as though there was atrophy of the fatty layer. He thought the case very interesting.

Dr. Ormsby thought the case did not correspond to any of the cases recorded.

A CASE FOR DIAGNOSIS. Presented by Dr. Stillians.

The patient was a Jewess, aged 45 years, who had a disorder of the nails which had been present for the past three months. There was swelling of the nail folds with darkening and roughening of the outer side of the left index, second and third fingernails. The same condition was just beginning on the right thumb nails.

There was a history of one miscarriage ten years ago. Four children were living and well, 16 to 25 years of age. Following a pelvic operation four years ago the patient had been having the menopause and complained of stinging, tingling sensations in the fingertips at times.

The Wassermann reaction was negative.

The nail folds of the left index, second and third fingers were swollen and pinkish-red. The nail of the left index finger was cross-ridged and black. The other affected nails had a greenish-brown streak along the outer side, where the nail was rough and splitting.

DISCUSSION

DR. ORMSBY asked whether the patient had used ammoniated mercury ointment on the nails and thought the appearance of the nails suggested that she had. The rest of the condition he considered onychia.

DR. STILLIANS stated that the woman asserted that she had used no medicine. He was interested to know why the nails were dark along one border. The paronychia seemed to be well over the whole base of the nails, but the discoloration was only along one side. He thought the condition might be due to a local irritation but could not understand the involvement of only one side.

A CASE FOR DIAGNOSIS. Presented by DR. MCEWEN.

The patient had been seen only a short time before being presented, and a full history was not yet available. The facts so far secured were briefly: The patient, a man, 36 years old, was tabetic; for a number of years he had been employed in an iron foundry where, in connection with the process of case-hardening, he had come in contact with sodium cyanid. As a result of this (he stated) he had had much irritation about the genitalia and buttocks for which he had received a great deal of treatment, without avail. These lesions occupied the lower part of the back, the buttocks, the groins and lower part of the abdomen; they consisted of poorly defined, reddened areas, some showing excoriations, others crusting, others presenting grouped vesicles. Recently, on account of some symptoms connected with the tabes, he had consulted the department of neurology where he had been given potassium iodid. About one week after beginning this medication new lesions, acneiform and urticarial in type, appeared on the arms and trunk; the older lesions also became aggravated.

The case was presented with the following queries: What was the original eruption? Had potassium iodid any part in the present skin condition?

DISCUSSION

DR. FROST thought that possibly an iodid eruption was intensifying some previous eruption.

DR. FINNERUD considered it a case of dermatitis herpetiformis. The location was right for this disorder as were the lesions.

DR. FOERSTER believed it was erythema multiforme without any symptoms of constitutional character. The history of the recurrence of a similar eruption during a period of three years without the ingestion of potassium iodid he believed would help out in the diagnosis.

DR. BAER thought it was dermatitis herpetiformis and said that the lesions over the sacrum were distinctly of that disease.

DR. SENEAR believed it was dermatitis herpetiformis and that the question of iodids playing a part in the present attack could not be definitely decided. If the fresh erythema-multiforme-like lesions and some of the somewhat urti-

carial-like lesions were a new feature the potassium iodid, he thought, might have been a factor in their production, but the whole picture was that of dermatitis herpetiformis.

Dr. Ormsby thought it was a well-known fact that certain cases of dermatitis herpetiformis exhibited lesions similar to those of multiform erythema. He had seen such cases frequently. In his opinion the case undoubtedly was one of dermatitis herpetiformis which in the present attack exhibited lesions of the multiform erythema type.

Dr. McEwen said his opportunity for examining the patient had been brief, and he had not considered dermatitis herpetiformis, although he agreed that it must not be omitted from consideration. He had thought the idea of a dermatitis venenata associated with the man's work offered a reasonable explanation for the persistent dermatitis. Some of the lesions had been present most of the time for three years, but those on the abdomen and forearms had appeared within the last week and seemed to be associated with the ingestion of potassium iodid. The patient had thus far received no benefit from treatment of the older lesions. He would try to keep the patient under observation and present him again at a later date.

PEMPHIGUS. Presented by Drs. Ormsby and Mitchell.

A man, aged 39 years, who was first presented before the Society in May, 1921 (*Arch. Dermat. & Syph.* 4:284 [Aug.] 1921), had received all sorts of treatment with no apparent change in the lesions. Thorough physical examination by all known methods had failed to reveal any pathologic condition.

DISCUSSION

Dr. Foerster said that when he saw the patient a year or so ago he thought the case belonged in the pemphigus group. It was an exudative, mild suppuration of the skin, distinctly in the pemphigus group.

Dr. Senear agreed with Dr. Foerster. He recalled a patient with acquired epidermolysis bullosa who developed the characteristic bullous lesions at the sites of trauma while over the back and trunk there were flat bullous lesions which closely simulated these, and he thought this substantiated Dr. Foerster's idea of the pathology in this case.

Dr. Ormsby stated that he had kept the case under observation but had not been able to arrive at any conclusion. It was a syndrome he had never seen before and which was resistant to all treatment.

PARAPSORIASIS. Presented by Dr. Stillians.

A student, aged 21 years, noticed two scaly red patches on the glans penis three and a half months ago, which were accompanied by slight itching. Since that time red spots had appeared on the trunk, arms and thighs which had become scaly and slightly itchy. Maculopapules, pink and not sharply defined, were present on the left forearm. On the trunk and thighs a number of scaly, maculopapules, light red and with small scales were seen. There were some slight stains left by former lesions and a number of scaly macules of normal skin color were present. The Wassermann reaction was negative.

The patient had used a mild salicylic, sulphur and resorcin zinc paste, without benefit.

DISCUSSION

DR. FINNERUD said he did not know what relation the lesion of three and a half months ago had to the present eruption, but thought it was one of the persistent pityriasis rosea eruptions. Some of these cases he had thought were seborrheic dermatitis, but he had become convinced that all of them were in the pityriasis rosea group.

DR. ZEISLER said he had seen many cases of pityriasis rosea that were very similar to this.

DR. ORMSBY stated that a few years ago the late Dr. Harris presented several cases before this society as unusual examples of pityriasis rosea. This patient presented similar lesions to those presented at that time and his lesions were probably identical with them.

DR. SENEAR agreed that it was pityriasis rosea. It was not a typical picture, but the characteristic arrangement of the eruption made him feel that it belonged in this group.

DR. STILLIANS said when he first saw the patient he thought it was a case of pityriasis rosea, but he had since wondered whether it could be a parapsoriasis. He would keep the patient under observation and report later.

LICHEN PLANUS, ATYPICAL. Presented by DR. STILLIANS.

About Aug. 1, 1921, one bright red, dry, round, pimple appeared on the inner side of the right leg just below the knee of a woman aged 31 years. Others soon followed, forming a group; then another group appeared on the outside of the right thigh about September 1, and about three weeks later a spot appeared on the left palm.

At the time of presentation there was a circular group of about twenty discrete, brown-red papules of various sizes, and small pigment stains at the site of former lesions could be observed below the right knee. On the outside of the right thigh several similar papules were arranged in lines; back of the right ear was a linear group, on the left palm a single flat nodule with a scaly, sunken center, and below the left ankle a flat, brown papule covered by adherent white scales.

These lesions all showed brown under the diascope, but were not translucent. Slight itching was present at times.

DISCUSSION

DR. SENEAR called attention to the distinctly apple jelly-like nodules present on the leg, and the lesions there resembled closely those in the patient presented by Dr. Pusey as having a case of acnitis, and which many of the Society thought to be follicular lupus vulgaris. That condition has since cleared up considerably under the use of lotio alba and calamin lotion. Examination of Dr. Stillians' case also suggested lichen planus in spite of the distribution of the eruption. Some of the lesions were distinctly angular, and the ones on the wrist he thought were umbilicated. He believed both of these conditions should be considered.

DR. MCEWEN thought it was a case of tertiary syphilis. The color and grouping he believed made this diagnosis probable.

DR. ORMSBY was unable to convince himself that there were any nodules. He had made pressure with the diascope and thought there were no apple jelly nodules present. He thought it belonged to the group of rather superficial late nodular syphilids.

Dr. Finnerud believed it was one of the superficial syphilids and said he saw a case very much like this one last year, which proved to be syphilis.

Dr. Stillians said he had considered tuberculid, but while the lesions were dark under pressure they were not translucent. He thought the case was an atypical lichen planus. He had not as yet made any tests but would try to get a biopsy and Wassermann test and report later.

A CASE FOR DIAGNOSIS. Presented by Dr. Stillians.

The patient was a Jewish tailor, 35 years old. In 1919, several small, soft, white papules appeared in the left palm. Under treatment advised by a druggist all but two of them disappeared. Two lesions persisted, and in July, 1921, began to discharge pus, and several others appeared, forming a group which had persisted in spite of various kinds of treatment, but had become dry and had decreased slightly in size since receiving a one-fourth erythema dose of roentgen rays on Oct. 8.

Toward the ulnar side of the left palm a group of rounded nodules could be observed, separated by deep fissures, with some irregular crusts. The group measured 2 by 3 cm. and had a polycyclic border.

DISCUSSION

Dr. McEwen thought it was a granuloma pyogenicum.

Dr. Baer and Dr. Senear agreed with this diagnosis.

Dr. Zeisler thought the lesions were not vascular enough for a granuloma pyogenicum, but had no diagnosis to offer.

Dr. Stillians thought it was a dermatitis vegetans. The lesion was peculiar, with rounded nodules. Cultures had revealed nothing but staphylococcus.

A CASE FOR DIAGNOSIS. Presented by Dr. Zeisler.

A woman, aged 45 years, had an eruption of the hands and face which had been present for three years. The lesions on the backs of the hands were dry and squamous, some of them excoriated, as were some of the lesions on the face.

When seen in the dispensary a year ago someone had made a diagnosis of dermatitis factitia.

DISCUSSION

Dr. Stillians thought the lesions were neurotic excoriations.

Dr. Zeisler agreed.

SARCOID. Presented by Dr. Stillians.

A colored man presented before the Society at the April meeting, 1920 (*Arch. Dermat. & Syph.* **2**:122 [July] 1920), since that time had had many tiny flat papules, a group of papules at the corner of the mouth and a number of tiny papules following the rim of the nares on either side. Roentgen examination of the hands revealed no changes in the bones except a slight thinning of the cortical border.

DISCUSSION

Dr. Ormsby asked whether Dr. Stillians was satisfied that it was a case of sarcoid. He thought the lesions on the face were a good example of lupus miliaris of the face.

DR. STILLIANS said he had presented the case again on account of the many tiny, flat-topped lesions which had appeared. He did not remember this in any case of sarcoid. No tubercle bacilli had been found at the first examination, but he would search again. The presence of superficial and subcutaneous lesions in the same case he considered of interest.

BLASTOMYCOSIS. Presented by DR. STILLIANS.

A Pole, aged 60 years, a laborer, had had the disorder since September. The condition appeared suddenly like a small pimple and progressed rapidly to tumor formation. Blastomyces were found in the pus. There had been marked improvement under neo-arsphenamin treatment, but no improvement on potassium iodid alone.

DISCUSSION

DR. MCEWEN asked whether there were any systemic evidences of lesions.

DR. STILLIANS thought the case interesting because they had two cases almost exactly like it under observation at the present time.

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